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PHYSICAL MEDICINE AND REHABILITATION FOR THE CHRONICALLY ILL

FRANK H. KRUSEN, M.D.

Section of Physical Medicine and Rehabilitation, Mayo Clinic, Rochester, Minnesota

Chronic illness and the medical problems of the aging are increasing enormously. More extensive general employment of physical, mental and social rehabilitation of the chronically ill is of the utmost importance. All of us must abandon an attitude of passive acceptance and neglect of chronic illness and substitute an attitude of optimism and vigorous dynamic rehabilitation of aged and chronically disabled persons. Physicians and laymen alike should support the development of the fascinatingly interesting new phase of medicine, known as physical medicine and rehabilitation, in the management of patients handicapped by chronic illness or injury. Proper rehabilitation of the chronically ill will result in enormous benefits both to patients and to the community.

Because of the tremendous difficulties encountered in the management of acute illness and the saving of lives, we physicians and also the public at large have been prone to put off and to neglect our obligations in relation to the rehabilitation of persons having chronic illness. Yet, practically everyone will encounter sooner or later the tragedy of dealing with the chronic illness of a beloved wife, husband, parent or child. Therefore, we cannot now continue the previous national tendency to accept passively and to avoid concern with the rapidly growing problem of chronic illness.

Anyone interested in chronic illness may profit by a careful study of the extensive five-volume report of the controversial "President's Commission on the Health Needs of the Nation" (1). Although I cannot agree with many of the recommendations of the Commission, particularly with those which concern enormous increases in expenditure of federal funds, I believe that much of the survey material is factual and worthy of consideration.

All of us who are interested in improving the health of the citizens of this nation should put aside political considerations and study the report carefully, accepting that which is factual, logical and in the best interest of humanity, and rejecting that which is not considered to be good for our nation. This is the democratic way of doing things in this land of free speech. Hereafter, I shall refer to the "President's Commission" simply as the "Commission."

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If one excludes the recommendations of the Commission, many of which I personally would modify, it will be found there is much important information available on chronic illness and on rehabilitation. Most of these factual data confirm my major theme which is as follows:

We should support the challenging new concepts of dynamic physical, mental and social rehabilitation, instead of the traditional passive acceptance and neglect, in managing the increasingly serious problems of chronic illness—thus achieving great benefits to chronically sick or disabled persons and to the community.

The medical problem of chronic illness is a major one and, because it is increasing, it deserves as much, if not more consideration than does the problem of acute illness. Until recently, and to a certain extent even now, physicians have devoted their major attention to the causes, diagnosis and cure of acute diseases. Efforts in this direction have been outstandingly successful, and the life span of the average person has been extended from forty-nine years in 1900 to approximately seventy years today. In 1860 there were only 860,000 people in America who were more than 65 years of age. By 1950 the number had risen to 11,270,000, and by 1980 there will be 22,000,000. Now the life expectancy of people who have reached 65 years of age is thirteen years. This indicates that problems of chronic illness among elderly persons will increase and will be of long duration.

During the past fifty years, extraordinary progress has been made in the management of acute illness and in reducing mortality in our country. Now we need similar progress in the management of chronic illness. A number of infectious diseases such as typhoid fever and the principal communicable diseases of childhood (measles, scarlet fever, whooping cough and diphtheria) have been all but wiped out as causes of death. The death rate for tuberculosis has been cut by about 90 per cent and the record for pneumonia is almost as impressive.

Because of these improvements in the management of acute illness, we find now that we have produced for ourselves a wholly new group of problems in relation to chronic illness. Our success in postponing death has led to the necessity for management of an ever-increasing number of chronic illnesses and serious disabilities. We have saved many chronically ill and seriously injured persons from death, but there can be worse things than death. It may be much more humane to provide services which will save chronically ill or seriously disabled persons from years of dependency than to save their lives.

Every time modern medical ingenuity and surgical skill in the management of acute illness save the life of a young man who would previously have died of an extensive and seriously crippling automobile injury, and every time the use of a respirator or a tracheotomy preserves the life of an extensively paralyzed child during the acute phase of poliomyelitis, physicians have triumphed over death, but they have also made for themselves a new problem in chronic illness and in providing facilities for the physical, mental and social rehabilitation of a living but seriously disabled patient. To restore such a patient so that he can return to self-respecting citizenship is a medical responsibility of the utmost importance, and we should be bending every effort toward solving the problems of the increasing number of seriously disabled and chronically ill patients.

The Commission has pointed out that "great backlogs of need have accumulated, and are being increased daily because insufficient attention has been paid to prevention of chronic disease and to rehabilitation of persons already disabled . . . the total number of individuals with some sort of known physical or mental impairment has been estimated as about 28,000,000." Almost 4,000,000 of these persons are invalids or are disabled for long periods. The Commission has added, "The first principle is that the care of the chronically ill must be brought up to the standard of the care given to persons with acute illness. Shoddy facilities that are still being used for the care of the chronically ill and the shabby attitudes that still characterize a part of the general public and a rear-guard of professional groups can no longer be tolerated."

The second principle is that "The care of the chronically ill is inseparable from general medical care, that one weaves through the other. Therefore facilities and services for the chronically ill should be planned in close administrative, professional and geographical affiliation with general hospitals and, where feasible, with medical schools."

The third principle is that "The needs of the chronically ill are so varied that facilities and services must be planned for the patients to move easily from home to hospital to nursing home and vice versa." I subscribe most heartily to all three of these principles as laid down by the Commission. Dr. Robert N. Barr (2) of the Minnesota Department of Health, has said, "There is an urgent need for the promotion of an educational program in the field of chronic illness with particular emphasis on the value of rehabilitation and the need for additional rehabilitation facilities."

The members of still another group, the Commission on Chronic Illness (3), not to be confused with the "President's Commission," have asked the most important medical question of the day when they inquired, "Can vigorous attacks on the chronic diseases be as successful as the efforts of the past few decades to reduce acute illness?" Prevention of chronic illness was made the cornerstone of any future program during the first conference of this Commission. However, there are many types of chronic illness that are just as inevitable as death itself and like death, they cannot be prevented, they can merely be postponed. The Commission has wisely turned its attention to planning another conference on the care of the chronically ill. Care and rehabilitation are just as important as prevention because, in many cases of chronic illness, we must devote major attention to the physical, mental and social rehabilitation and to the training of patients to live, with the greatest possible happiness, despite the fact that they have certain inevitable chronic diseases.

Proper understanding and the use of physical medicine and rehabilitation are of first importance in managing chronic illness and in limiting or postponing disability caused by chronic illness.

Physical medicine has been defined as the employment of various physical agents and devices, therapeutic exercises, corrective procedures, occupational therapy and physical rehabilitation in the diagnosis and treatment of diseases and injuries.

General Paul R. Hawley has said (4), "Formerly the objective of physical

medicine was limited to the restoration of function of injured parts. The experience of the war showed that usually the whole man is affected adversely when one part of his body is disabled for more than a brief period. This adverse effect often is mental as well as physical. Consequently, the field of physical medicine was expanded into rehabilitation." Thus physical medicine and rehabilitation have become inextricably conjoined, under the guidance of the new specialty of physical medicine and rehabilitation, which now has its own specialty board, its own council and its own section in the American Medical Association.

Rehabilitation has been defined by the Commission as "the restoration through personal health services of handicapped individuals to the fullest physical, mental, social and economic usefulness of which they are capable, including ordinary treatment and treatment in special rehabilitation centers." H. E. Griffiths has said (5), "Rehabilitation is treatment, but it is not the treatment of disease or injury, but the treatment of the individual suffering from the disease or injury." Henry Kessler (6), one of the great medical leaders in rehabilitation of the disabled, has said, "Rehabilitation has acquired new connotations growing out of civilian and military experience. It has come to be regarded as a creative process in which the remaining physical and mental capacities of the physically handicapped are utilized and developed to their highest efficiency. It is an organized and systematic method by which the physical, mental and vocational powers of the handicapped individual are improved to the point where he can compete, with equal opportunity, with the so-called non-handicapped."

Even some of our keenest observers have not fully understood the implications of modern physical medicine and rehabilitation and then have suddenly come to the realization of the manner in which the chronically ill are now being restored to suitable vocations. Thus, after studying the work of one center of physical medicine and rehabilitation, David Hinshaw said (7), "I had missed the emergence, through it, of the miracle of the composite science of rehabilitation. Suddenly I realized that its staff was using medicine and surgery, therapy, psychology and psychiatry, patience, kindness, friendly understanding, and vocational training in their efforts to help the physically handicapped re-educate themselves, to live and work and love by enlisting their minds, hearts and bodies." The Commission has reported that approximately 2,000,000 persons have disabilities requiring rehabilitation services to make them employable. Of this group, approximately a fifth (400,000 persons) are estimated to be so severely handicapped that comprehensive rehabilitation services and specialized facilities are considered necessary. Each year, as a result of disease or accident, about 250,000 persons of working age become in need of rehabilitation.

Very significant is the observation of the Commission that "Military and other injuries dramatized the problem of disability and finally forced legislative and remedial action, but the major cause of handicapping is chronic disease. Chronic disease accounts for 88 per cent of all cases which could benefit from rehabilitation." Congenital conditions account for 2 per cent, occupational accidents, and injuries for 5 per cent and other accidents, including those in the home and on the highway, for another 5 per cent. But disease supplies the steady backlog of incapacitation.

This is the key statement concerning the relationship between chronic illness and the need for physical medicine and rehabilitation in our general hospitals. I should like to reiterate that proper management of chronic illness can best be achieved by proper coordination of physical medicine and rehabilitation (conducted by physicians) in general hospitals with vocational rehabilitation (conducted by social workers and educators) in voluntary agencies and state departments of welfare and education.

Physicians and the public must change their traditional attitude of passive acceptance and neglect of chronic illness and place physical medicine and rehabilitation for the chronically ill on the same level with medicine and surgery for the acutely ill. Until recently, most general hospitals have been reluctant to provide adequate numbers of beds for the care of the chronically ill. They are anxious to serve those who are acutely ill but, mindful I suppose of the danger of filling many expensive beds with patients who will be ill for a long time, they have been reluctant to provide suitable services for handicapped persons who are chronically ill or disabled. I have long advocated that every department of physical medicine and rehabilitation in the general hospital shall have its own bed service, not for the domiciliary care and vegetation of a group of patients with permanent disability, but for the vigorous and dynamic restoration of such chronically ill persons to the fullest possible physical, mental and social productivity and usefulness.

The Commission has said, "A great need exists, for the establishment of departments of physical medicine and rehabilitation in general hospitals where patients with acute cases and with residual difficulties can achieve treatment." They said that the average community hospital of 200 beds or more could profitably set aside perhaps 20 per cent of its beds for convalescent and rehabilitation care. I fully concur in this important observation.

Properly conducted, the care of patients in a chronic disease unit can be much less expensive than the care of the acutely ill. R. K. Fox (8), of St. Luke's Hospital, Duluth, has reported that the cost of the chronic disease unit is $6.53 per person per day, which is about a third of the cost for the care of the acutely ill in this hospital.

In an active hospital service for rehabilitation of the chronically ill, the patients should not be kept continually in bed. On the contrary, they should be kept active throughout the day. The Commission said, "Where institutional facilities are used, these should strive to incorporate the features of a pleasant family home."

I have long decried the habit of hospitals in requiring most patients to remain completely inactive in bed, thus permitting them to become morbid and introspective, and actually delaying their physical and mental recovery. Nearly a decade ago I recommended (9) what then seemed a startling innovation, the permitting of hospital patients to become ambulatory, to engage in social activities, to pursue recreational programs, to be provided with a theater or hall, a public address system, a library, a gymnasium and even in some instances a swimming pool. Now the Commission has observed, "The hospital of tomorrow should be a well-rounded health center from which preventive, diagnostic, treatment, reha-

bilitative, and home care services radiate to the entire community . . . It has been proved that a rehabilitation unit in a hospital can speed appreciably the discharge of patients. There is need for much wider use of these units in major hospitals."

Let us imagine that you have a child suffering from poliomyelitis with residual paralysis, or a parent who has had a stroke with resulting paralysis. Would you like that person, who is very dear to you, to remain in your community hospital only until the acute phase of his illness is past and he can get out of bed, and then see him forced to seek to rehabilitate himself as best he can, or would you prefer to have this paralyzed child or parent seen by a competent rehabilitation team when he first enters the general hospital and to have that team (working as a unit of the general hospital staff) help him to get out of bed, train him in the use of his paralyzed limbs, assist him with his psychologic problems, and move him as soon as possible from the section of the hospital devoted to acute illness to a home-like convalescent section, where his clothing would be restored to him and he would be assisted in learning the activities of daily living once more?

Here he would be kept busy on a schedule of physical therapy, occupational therapy and recreational, avocational and pre-vocational activities. The child would be permitted to attend a hospital school to continue his education during his prolonged convalescence. Either the child or the adult could, when he was able, go out with a group of other convalescent patients to attend the theater or a sports event. Both might join in the writing and the printing of the patients' own news bulletin. Either might be permitted to go home for the week end and then to return to his active program of rehabilitation on Monday morning. Both would find the atmosphere congenial rather than forbidding.

Each of these patients would continue to be followed by the hospital's whole team of medical advisers, including his own "family doctor," the internist, the pediatrician, the neurologist, the psychiatrist, the orthopedist and the physiatrist, right through the convalescent period. Both would achieve far more rapid recovery than was formerly possible. I know that this is feasible because we have such a service run by the Section of Physical Medicine and Rehabilitation of the Mayo Clinic at St. Marys Hospital in Rochester, Minnesota. Increasing numbers of hospitals are finding it possible to achieve more rapid rehabilitation of seriously disabled patients by following such a plan.

The Commission reported, "In November, 1950 a physical medicine and rehabilitation department was established at Gallinger Hospital in Washington, D. C. . . . During the year prior to the formation of this new department, orthopedic cases spent an average of fifty-five days in the hospital. During the first year of operation of the new program, the average length of stay of the orthopedic case dropped to thirty-three days."

The novelty, and the departure from the traditional, which characterize this type of hospital program may produce an unfavorable reaction at first, yet it has been shown that the suggestions are wholly rational and not radical.

The religious philosophy of that great physician philosopher, Albert Schweitzer (10), might well guide us in planning new programs for the rehabilitation of

the chronically ill. Schweitzer said that man must liberate himself from the overpowering domination of mass institutions. He must learn to think for himself and to judge for himself what is good and what is bad. He must always bear in mind the "will to live" of his fellow men. He said, "It is good to maintain and encourage life; it is bad to destroy or obstruct it." According to this philosophy, all of these steps which maintain and encourage life are good.

The Commission on Chronic Illness has pointed out that one of the greatest needs is to change attitudes toward chronic disease. It is seeking for means to influence people to understand that chronic disease is not necessarily hopeless, to educate the public to lead the kind of life that reduces the danger of acquiring chronic disease, to train everyone to seek early detection of disease, and to aid those who have a chronic disease to make the best possible adjustment to it. Finally, the Commission is seeking means of influencing the professions to give as much interest and attention to chronic disease as they now give to acute illness. If all of us would adopt the philosophy of Albert Schweitzer, the task of this Commission on Chronic Illness would be much easier.

Every effort should be made to increase the number of specialists in the fascinatingly interesting new branch of medical practice known as physical medicine and rehabilitation. The Commission, although urging the establishment of departments of physical medicine and rehabilitation in general hospitals, pointed out that "One of the most serious obstacles facing hospitals interested in establishing such a department lies in the extreme shortage of specialists in physical medicine." The Commission added, "In view of the fact that the American Board of Physical Medicine and Rehabilitation was created as recently as 1947, the number of physicians certified in physical medicine and rehabilitation is extremely limited. Currently there are 170 diplomates of the American Board. Estimates indicate that between 2,500 and 3,000 additional physiatrists, specialists in physical medicine and rehabilitation, are needed."

It was my privilege to serve as one of the founders and first chairman of this board, and I know how true these statements are. I wish from the bottom of my heart that I could inspire many more young physicians to enter this specialty because, after nearly a quarter of a century of specialization, I find it just as fascinating and just as challenging as when I first started to work in this field in 1929. This specialty gives the young physician the opportunity to pioneer in the American tradition. It offers amazing opportunities to fulfill one's creative urges. It provides the privilege of extending medicine into new frontiers of humanitarian endeavor. It extends new vistas for laboratory and clinical research. It is truly one of the frontiers of medicine. Right now, there are innumerable openings in rehabilitation centers, and 20 medical schools are seeking qualified physiatrists to develop departments and teaching programs in physical medicine and rehabilitation. The Commission reported that as of June, 1951, in the Veterans Administration alone, "there were vacancies for fifty-six chiefs of physical medicine and rehabilitation." The Commission added, "The approximately ninety approved residencies available in physical medicine and rehabilitation offer encouraging evidence of educational progress when one considers that eight years

ago, only five approved residencies were offered. In eight years the output of new specialists in this field has increased from three or four a year to forty or fifty a year. Yet, to meet the present needs of 2,500 to 3,000 additional physiatrists, we should be training several hundred a year for many years to come."

One of my major efforts has been to train young physicians to head teaching departments in our undergraduate medical schools, and I agree with the Commission when it says, "Expansion of the teaching of physical medicine and rehabilitation in the undergraduate curricula of medical schools can serve a dual purpose. It can prepare the prospective physician to incorporate rehabilitation concepts into the future practice of whatever aspect of medicine he chooses. It may also serve to interest the undergraduate student in selecting the specialty of physical medicine and rehabilitation."

It is my devout prayer that many more students will select this specialty during the years to come. Also, it is to be hoped that all physicians, those in general practice and those in other specialties, will learn to understand more fully the concepts of physical medicine and rehabilitation. The Commission has pointed out that "It must be part of the daily working armamentarium of each physician. . . . Many hospitals, schools and medical centers could with profit practice rehabilitation as a part of the enlarged concept of medical responsibility."

All of us (physicians and public alike) should support the new concept of dynamic physical, mental and social rehabilitation in providing suitable management of chronic illness. The modern approach which includes, in the rehabilitation of patients with chronic illness, psychologic and social as well as physical restoration is constantly coming to the fore. Recently, Dr. Lester Evans (11) of the Commonwealth Fund, in discussing "The Next Twenty Years in Medicine," concluded that teaching and research centers must learn to co-ordinate their activities "if modern medicine is to deal with man as a whole." If we consider not only the physical aspects of disablement and chronic illness but also the social and psychologic aspects, we can develop a form of hospital practice which, according to Evans, will have "its roots in the lives and needs of the people."

In a new book by Max Pinnar and Benjamin Miller entitled "When Doctors are Patients," (12) a group of physicians have described their various personal experiences with their own different serious diseases. It is a revelation to discover that almost every one of these physicians, as he recited the problems he faced in dealing with his own illness, stressed the psychologic and social aspects of his disease. As was pointed out by one of the editors, Dr. Pinnar, "This emphasizes in a peculiarly urgent and moving way how essential it is to treat the whole patient."

In rehabilitation of the chronically ill, we should be giving ever-increasing consideration to this philosophy of treating each patient "as a whole" and to the importance of considering not only the physical but also the psychologic and social aspects of the illness of each chronically disabled patient.

A broadening of our medical concepts which recognizes that it is the obligation of the physician and the hospital to take the lead in caring for each patient from

the beginning of his illness or injury until he is restored physically, mentally, socially and economically to the fullest possible productivity, is apparent. To meet and to fulfill this new conception, our general hospital departments of physical medicine and rehabilitation, and particularly those connected with teaching centers, must develop combined programs of good practice, proper teaching and satisfactory research.

Practice may be fairly extensive. In our experience at the Mayo Clinic, 11.5 per cent of all of the patients coming to the clinic are referred to the Section of Physical Medicine and Rehabilitation.

Proper teaching can be carried out only by a qualified specialist who is equipped with a well-organized department in which to do his teaching. The unfortunate recent tendency of certain medical educators to contend that new phases of medicine should not be taught in separate courses but rather that they should be "integrated into" or "co-ordinated with" existing courses, is, in my opinion, tending to retard the development of new specialties such as my own. In 1871, President James A. Garfield (13) told the alumni of Williams College, "Give me a log hut, with only a simple bench, Mark Hopkins on one end and I on the other, and you may have all the buildings, apparatus and libraries without him." At that time, President Garfield enunciated a profound truth which, in the complexities of modern medical education, is perhaps too frequently overlooked. The best way to teach any subject is to provide at least one good teacher of that subject. We must let our few experienced men in this field teach the subject completely and directly to the undergraduate students. It is to be hoped that, among them, there will be a few men who approach the caliber of Mark Hopkins.

Research will form the basis for all advances which will come in the field of rehabilitation of patients with chronic illness. According to Dr. Alan Gregg of the Rockefeller Foundation (14), "The word 'research' has a flavor of dissatisfaction with the search made hitherto, or with hitherto accepted explanations . . . . The research involves betimes a critical examination of our sources and ways of learning what we describe as facts." This is the age of physics, and research in physical medicine includes various applications of biophysics to the treatment of disease. Already physiatrists have made intensive studies of two of the great weapons of war, radar and sonar, and have converted them to the service rather than to the destruction of mankind, by utilizing radar as microwave diathermy and sonar for ultrasonic therapy and diagnosis.

Clinical research during and since World War II led to the recognition of the importance of physical medicine and rehabilitation in the care of our wounded soldiers and sailors. For example, clinical research in new methods for rehabilitation of paraplegics led Major General Norman Kirk (15), the Surgeon General of the Army, to write, "Until this program was instituted, men with spinal cord injuries and resulting paralysis were regarded as hopeless invalids and I fear that they were treated as such. The attitude has been completely reversed. . . . To get the patient out of bed and on his feet was the goal in every paraplegic center for every man treated in it. We hitched our wagon to the stars and we got where we were going in a surprising number of cases."

There are many indications that the medical profession is achieving new goals through laboratory and clinical research in the fields of physics as applied to medicine and in the rehabilitation of the disabled. The Commission on Chronic Illness has added, "Long term studies of the interplay of genetic constitution and environment should yield findings applicable to many chronic diseases. Similarly, further investigation of the role of emotional factors would also be applicable to many of the chronic diseases."

Adequate rehabilitation of the chronically ill will result in enormous benefits to these sick and disabled persons as well as to the whole community. The Commission reported that in West Virginia during 1951, "The disabled members of 376 families receiving public assistance were rehabilitated. These families were receiving annually about $225,000 in assistance payments. It cost less than this amount to rehabilitate them. Now they are not only off the public rolls but they are earning about $500,000 a year." Thus not only the person who is chronically ill but also the community is benefited.

I agree thoroughly, however, with the Commission when it said, "The economic argument for rehabilitation work is a strong one, but the real goal is not a saving of dollars and cents. The real goal is human values. Saving life and enabling it to do the heretofore impossible requires depths of courage and brings out new well-springs of satisfaction. Everyone is heartened by what the handicapped can do in the face of really great difficulties. In performing miracles of adjustment, they help keep others from succumbing to the small and trivial things of life."

CONCLUSIONS

My theme is that we should support the fascinating new concepts of dynamic physical, mental and social rehabilitation, instead of the traditional passive acceptance and neglect, in managing the increasingly serious problems of chronic illness, thus achieving great benefits to chronically sick or disabled persons and to the community.

The Commission concluded, "Adding to leadership in other aspects of medicine, a superiority in rehabilitation technics could bring new reserves of strength to this nation. Rehabilitation demands a highly developed form of cooperation and certain ethical ideals. Only in a democracy is there any future for growth and life, in which everyone, even the handicapped, have a chance. In helping the handicapped, we strengthen not only the health but also the moral fiber of the nation."

The Director of the Office of Vocational Rehabilitation, Miss Mary Switzer (16), has written, "Rehabilitation is a bridge spanning the gap between uselessness and usefulness, between hopelessness and hopefulness, between despair and happiness."

Our great and public-spirited philanthropist, Bernard M. Baruch (17) who has done so much to aid in the rehabilitation of the chronically ill, has said, "The investment in rehabilitation is an investment in the greatest and most valuable of our possessions, the conservation of human resources."

Now we must labor to make longer life bearable for all patients having chronic

illness. Today it is the physician's responsibility not only to add years to life but also to add life to years.

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STEROID HORMONES IN GERIATRICS

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INTRODUCTION

Man has, since the early historical periods, tried to stay the inevitable hand of time. Down through the ages he has dreaded and lamented the oppressive hand that slowed his gait, dulled his senses, bent his back, and whitened his hair as a prelude to snatching him into oblivion. He has sought after, dreamed and written of ways to waft himself back to the vigorous vital days of his youth.

The view of medical men of past ages has been one of helplessness in the face of the inescapable. They sadly shook their heads and resigned themselves with other men to the debilitating effects of the aging process. It may be said that to the French scientist, Brown-Sequard, goes the distinction of being one of the first to attempt to deny Father Time his due, through the use of steroid hormones. He injected himself with extracts of bull testes in the hope of rejuvenating himself. Because of the small amount of androgen which he actually received from these extracts his experiments were unsuccessful, but modern medicine has proved his theory sound. Steroids do have the power to reverse some of the pathologic changes of aging.

Steroid hormones are those possessing as a common structural base the perhydro-cyclo-pentano-phenanthrene nucleus. Differences in the placement of the ketone groups, side chain and hydroxyl on the basic phenathrene structure produce the hormones of the testis, ovary, corpus luteum, and adrenal cortex. These hormones are also closely related to some of the components of bile, cholesterol and vitamin D. Although used as replacement therapy in gonadal and cortical hypofunction, for over a decade, the use of steroids as specialized tools in geriatics has been a very recent advancement. This has been mainly because the field of geriatrics itself is very new. For only a few decades has much been attempted by the medical profession in the study and treatment of diseases of old age. Geriatrics as a specialized branch of medicine is even younger.

Geriatrics is defined as the branch of medicine which is concerned with the treatment of the diseases of old age. Such a definition immediately brings about the question "When does old age begin?" Examples like the spry, active man "70 years young" and the puffing, graying, arteriosclerotic of 40, make any precise age limit for geriatics purely arbitrary. Some authors maintain that in women the menopause, usually occurring between 45 and 50, is the point after which the decline of age sets in. Others set a much higher age limit. Fifty-five seems to be the age most generally agreed upon as the beginning of old age.

The myriad uses to which the steroid hormones have been put, even in a field as young as geriatrics, is amazing. For convenience, steroid therapy will be

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discussed under the headings: 1) uses of estrogens, 2) uses of androgens, and 3) uses of adrenal corticosteroids.

USES OF ESTROGENS

One of the major uses of estrogens is in postmenopausal pathologic conditions. The menopause signifies the decline and cessation of ovarian function. With this decline of the ovary, naturally there is a fall in the level of blood estrogen. Therefore the organs and tissues, particularly of the reproductive system, which depend upon estrogens to condition their functional processes must, after the menopause, live in an altered environment. This postmenopausal readjustment sometimes results in disorders of varying degrees of complexity. Many clinicians therefore believe that the low levels of blood estrogen seen in the postmenopausal period are the etiologic, or at least the predisposing factors for such conditions as kraurosis vulvae, pruritis vulvae and senile vaginitis (1). Kraurosis vulvae is an atrophic affection of the external genitalia characterized by whitening of the skin and literally a "shriveling up" of the normal folds. The epidermis becomes inelastic and parchment-like and cracks easily (2). Treatment by estrogen administration is very satisfactory. The estrogens may be administered orally (linguets), intramuscularly, or as vaginal suppositories or ointments in mild cases. The epidermis is returned to normal, the danger of infection diminishes and the patient is much more comfortable. Pruritis vulvae produces an intense itching and burning about the genitalia, which may spread to the anal and thigh regions. It may be continuous or intermittent, but in all cases the extreme discomfort of the patient is the concern of the physician. Pruritis vulvae has several causes, but when a decreased estrogen level is the etiologic agent, estrogen (by suppository, ointment or injection) brings gratifying relief. Atrophic vaginitis demonstrates still another result of estrogen deficiency. Irregular patches of vaginal epithelium are thrown off, forming erosions and adhesions. This condition, like the others described, regresses when estrogen therapy is begun. The atrophic mucosa is changed to the secreting type. The tissue atrophy precipitated by decreased estrogen levels of the postmenopausal period extends to include the urethra, sphincter, bladder and periurethral tissues. Atrophy of these organs brings on urinary symptoms of urgency and frequency of urination, dysuria and incontinence (3). Estrogens alleviate these symptoms by reversing the atrophic changes.

Of frequent occurrence in women of the postmenopausal age are articular disorders which cause pain and reduce the mobility of joints such as those in the hands, knees, wrists and neck. These disorders have been classed by some investigators as menopausal arthritis. Although writers take issue over the proper terminology, the fact remains that these joint conditions seem to stem from the altered gonad-pituitary relationship and decreased production of sex steroids resulting from the menopause. Two observations support such a theory. One is that the symptoms are ameliorated by administration of sex steroids. The other is that the symptoms, beginning at the menopause, progress to the unmistakable degenerative changes seen ten or fifteen years later. The differential diagnosis of

types of arthritic disease is beyond the scope of this paper, but encouraging success has been achieved with estrogenic treatment of the various forms of degenerative arthritis, osteoporosis and other arthralgias in female patients when the history traces the symptoms back to the time of the menopause (4). The same author has also reported successful testosterone therapy in male patients with degenerative arthritis when the history reveals clinical evidence of climacteric changes (4). However, due regard for neoplasms of the genitalia and breasts interposes a note of caution regarding such therapy. These arthritic conditions may be treated with gonadal steroids from the opposite sex; estrogen-androgen combinations are also of value (4), as is progesterone. The route of administration of these hormones is usually intramuscular or oral, but injections directly into the joint cavity have been successful.

Carcinoma of the prostate is another field for estrogen therapy. Baretz quotes Young as stating that 1 out of every 25 men who live past the age of 60 will have carcinoma of the prostate (5). These patients have greatly enlarged prostates which, in addition to being hazardous because of the possibility of metastases, cause painful pressure on surrounding organs. The most effective procedure is surgical removal, but the use of estrogenic compounds has had favorable results. The average dose is 2 mg. per day, although as much as 5 mg. daily may be administered. Estrogen administration produces extensive degenerative changes in the glandular structure of the prostate, which probably accounts for the decrease in the size of the gland in some patients so treated. However, these alterations are only temporary, and when the estrogens are discontinued the glandular structure again regenerates (6). It would seem, therefore, that the best use of estrogens in the treatment of prostatic carcinoma is in changing previously inoperable cases to operable ones, and in reducing the size of the prostate in order to relieve the pain. The mechanism of the action of estrogens can only be postulated at this time. They may act directly upon the prostate, indirectly via the anterior pituitary, or through alteration of the blood ratios of estrogens, androgens and gonadotropins (5).

In many elderly patients in whom massive doses of estrogens have been used, there has been the surprising observation of increased vascularity of the skin, increased numbers of cell layers, restoration of the normal wavy configuration of the epidermis and, in some cases, even the restoration of grey hair to its original youthful color (7). These are, however, side-effects, and estrogens should not be used for the sole purpose of achieving these results, because of the profound hormonal effects on the whole body. Estrogens also possess hematopoietic properties and can cause a distinct increase in the number of red blood cells, as will be discussed later. Estrogens are used for this purpose when their more powerful androgenic counterparts are contraindicated.

USES OF ANDROGENS

Androgens possess several properties of far greater importance in geriatric medicine than those associated with sexual activity. Their uses in some types of carcinoma, cachexia and a host of other clinical conditions make them extremely

useful geriatric tools. Of primary importance are the anabolic effects. Testosterone especially, produces a diminished excretion of nitrogen, inorganic phosphorus and sodium chloride. The retained ions are utilized for tissue rebuilding, which is promoted by testosterone and its related compounds. These androgenic and, to a lesser degree, estrogenic properties have been very valuable in preoperative and postoperative care. Elderly patients often present poor operative risks because of cachectic conditions and lowered physiologic reserve. Testosterone administration builds up muscle and connective tissue, increases glucose storage and generally enhances the clinical picture. Therefore, the patient is in better condition for the surgeon and the recovery period is shortened considerably. Administration of linguets of methyltestosterone to such patients has become routine in many clinics (8). The tissue-rebuilding properties of androgens are not, however, limited to peroperative and postoperative utilization. In the aged patient who presents a picture of debility associated with underweight, androgens (usually administered orally as linguets) will establish normal nitrogen balance and increase strength. (9)

Based upon experiments which indicate a favorable influence of testosterone on the circulatory system, this androgen has been reported to produce hypertrophy of the heart muscle (10). It is believed to have a favorable influence on the vascular tone of cardiac vessels. It may even reverse some of the arterial degeneration which occurs as gonadal function decreases (9). Even more important is the indirect effect upon the heart resulting from improved body and mental tone. The patient performs his tasks with less strain and effort, thus decreasing the cardiac burden. Patients in whom anginal attacks followed even minor exertion and in whom daily frequent doses of nitroglycerine were required for relief, have been given testosterone (5 mg. two to three times daily). It was found that they had better coordination and more self-confidence, there was no worry about being able to perform tasks which had before brought about effort reactions on the heart, and the strain of small exertions was reduced to normal (11).

It must be kept in mind, however, that the anginal state is not the result of a hormonal deficiency, and although patients may be benefited by androgen administration, the anginal state still exists and may be re-activated by overexertion. As in all hormonal therapy, it is well to keep in mind the old adage "a chain is no stronger than its weakest link." Likewise the elderly patient cannot be put into any better physical and functional shape than his aging cardiovascular system will allow. The ultimate results of building up muscular tone and renewing vigor and energy in a patient with aging arteries and low cardiac reserve are obvious.

Burnstein has reported on some experiments which may open the door to still more uses of steroids. He describes the supplementary treatment of diabetes mellitus with estrogens and androgens. These hormones suppress the diabetogenic pituitary principle in the same way that they suppress gonadotropic hormone production in the climacteric. When taken orally, they greatly reduce the amount of insulin required, thereby relieving the patient of the necessity of frequent injections. Supplementary steroid administration must be continued along with

the insulin therapy, because once the steroids are discontinued the insulin requirement returns to the pre-steroid level (12). Burnstein has also reported that in a group of 50 patients treated with testosterone he obtained up to two-thirds reduction in the insulin requirement (12). Such steroid therapy is especially good in geriatric cases, because it may be administered to men past 40 and women after the menopause without fear of inhibiting spermatogenesis and oogenesis.

It has been estimated that about 75 per cent of mammary cancers occur in women past the age of 40. The curve rises after the age of 40, so that the probability of cancer in women between 75 and 79 is ten times as great as between the ages of 35 and 39. Age in itself, therefore, is a predisposing factor. In cases of mammary carcinoma, particularly those in which irradiation and operative procedures have proved unsuccessful or dangerous, androgens have been used therapeutically. This field is still largely in the experimental stage, and consequently the procedures used to date have usually been empiric. The results obtained have been largely of a palliative nature, such as retardation of the spread of the cancer, production of a less fetid ulceration, and even successful preparation for surgery in many previously unoperable cases (13). However, some investigators have also obtained dramatic regressions of the cancer (14). The mechanism of the action of androgens in these cases is still a matter of speculation. Perhaps there is an overall enhancement of physiologic effects (8). Changes in the steroid equilibrium in the tumor-cell environment, the direct destructive action of androgen on the cancer cells and alteration in the body of androgen to a much more powerful anticancer steroid have all been postulated. Large doses ranging from 2,000 to 4,000 mg. per month are used. In women, the resulting masculinization is a drawback to this type of treatment.

Another recently discovered use of androgens shows great promise in geriatrics. Androgens and also estrogens have produced favorable results in the treatment of cutaneous disorders commonly seen in aging patients. Hollander and Vogel reported that patients have been completely cured of extensive areas of senile pruritis by the use of testosterone ointment (15). Other authors verified these findings with many other cases successfully treated for senile dermatoses, with androgens in males and estrogens in females (16). Bland ointments containing the sex steroids relieve the severe itching and burning and soon clear up the affected areas. Androgens have also been found to be of striking benefit in resistant eczema and fungus infections, especially of the feet (8). Whether or not relief in such cases is permanent has yet to be determined.

In using the sex steroids in large doses one of the most promising additional effects noted was that androgens possess definite hematopoietic properties. To a lesser degree estrogens exhibit the same properties. Use of testosterone in patients with refractory anemias has been surprisingly successful. In fact a polycythemia can result from the use of androgens over a long period of time.

In the infrequently observed male climacteric the symptoms are dramatically improved by androgen therapy. Because the atrophy and resulting hormonal inbalance believed to cause climacteric symptoms occur from five to ten years later in the male than in the female, the male syndrome is the concern of the

geriatrician. It is generally believed that the symptoms can be related to testicular hypofunction in the following manner. In the male at the height of sexual activity there exists a complex balance between the sex hormones and the gonadotropic factor of the pituitary. The gonadotropic factor induces androgen production and the androgens inhibit the anterior pituitary, thus limiting the amount of gonadotropic factor produced. When senile testicular atrophy begins, there is naturally a decrease in androgen production. This decrease reduces the inhibition on the anterior pituitary and an increased amount of gonadotropic factor is elaborated in an effort to obtain more testicular response. This great increase in the blood level of gonadotropic factor apparently causes the climacteric symptoms, especially those pertaining to vasomotor instability (17). Hot flashes, sudden drenching sweats, and excitability are the results of the unstable vasomotor system. Mental and emotional symptoms are probably the most frequent manifestations of the male climacteric (8). Such patients frequently suffer from severe spells of depression, worry over sexual impotence, loss of self-confidence, and extreme nervousness and irritability (18). Psychotic changes may be the underlying cause of some cases of suicide in men of advancing years. Administration of testosterone raises the level of blood androgen, inhibits excessive production of gonadotropic factor and restores to normal the ratios of these two hormones. Very quickly the hot flashes and sweats disappear. Physical and mental powers are increased and the patient regains self-confidence and an optimistic outlook. He sleeps well, becomes less nervous and is good humored. These results are prompt and definite (19). Such androgenic therapy can aid greatly in the patient's physical and mental adjustment to the limitations and potentialities of his new physiologic level of life, with a minimum of discomfort (20, 21).

USES OF ADRENAL CORTICOSTEROIDS

The steroids of the adrenal cortex regulate and influence so many of the body's vital functions that an evaluation of their therapeutic uses becomes extremely complex. It might be well, therefore, to discuss geriatric uses of these hormones in the light of some of their properties. Roughly the hormones of the adrenal cortex fall into four groups. There are the 11-oxysteroids, which possess in common an oxygen atom at C-11. They are chiefly concerned with carbohydrate metabolism in the body, and favor gluconeogenesis, particularly from protein. They also appear to promote the oxidation of glucose in the tissues. This property makes the 11-oxysteroids highly effective in postponing muscular fatigue. The desoxysteroids lack oxygen at the C-11 position. They control salt and water metabolism and regulate the body concentrations of sodium, potassium and water, thereby controlling tissue and cellular ionic and fluid content as well as plasma volume. The third fraction is the highly active, but as yet uncharacterized amorphous fraction. This fraction exerts an effect upon renal function and many other physiologic mechanisms. Lastly there are the cortical sex hormones. These estrogens and androgens contribute to the maintenance of the body's sex steroid balance.

Adrenal hypofunction, though not specifically a disease of the aged, is not

uncommonly seen in geriatric patients (20). It is best exemplified by Addison's disease. The grossly altered salt and water balance cause anorexia, nausea, vomiting, hypotension, and microcardia, and can lead to collapse with dehydration and circulatory failure (22). It must be constantly kept in mind that the adrenal corticosteroids exert a profound influence on all the tissues of the body. A curious antagonistic effect is also exhibited by some of these hormones. For example, whereas cortisone in high dosages halts the growth of granulation tissue and retards wound healing, desoxycorticosterone promotes exuberant growth of granulation tissue (8). It becomes obvious that therapy with these hormones should resemble the natural hormone elaboration in balancing salt-regulators against carbohydrate-regulators and healing-promoters against healing inhibitors.

As if spurred on by present achievements with corticosteroids, investigators have assayed them in many other diseases which are problems to the geriatrician. The potentialities of these hormones are overwhelming. We have just begun to see the corticosteroids as involved in certain types of allergy and hypertension, and in the abnormal metabolism of fats, proteins and carbohydrates (24). Corticosteroids can cause dissolution of certain types of lymphoid tumors, and they induce a remission, though temporary, in some forms of leukemia (35).

Of great importance to the geriatrician is the fact that corticosteroids bring about impressive amelioration in diseases primarily involving collagen, the chief constituent of connective tissue. The corticosteriods have received their most publicized usage in the treatment of rheumatoid arthritis, the outstanding collagen disease (8, 23). This disease generally begins in younger life, but its crippling effects last through the years, making it a geriatric problem also. The hormone is generally administered orally or intramuscularly and soon brings about a reduction in pain and an increase in joint mobility. Often when only one or two joints are involved, the hormone is injected directly into the synovial cavity. The anti-inflammatory properties of these steroids and their effect upon the abnormal collagen combine to bring about most gratifying relief to the patient. In the various forms of degenerative arthritis remissions have also been achieved with corticosteroids (21).

Wide gaps in our knowledge of the pathogenesis and etiology of rheumatoid arthritis create problems in therapy. The disease usually begins as an inflammatory reaction of the synovial membranes of the joint. It gradually involves the synovial sheaths, and adjacent tendons and bursae, and then destroys cartilage which, in more advanced cases, is replaced by bone (26). These pathologic changes are manifest to the patient by sharp pains in the joints and decreased ability to move them. The adrenal corticosteroids seem to reverse the degenerative synovial changes and prevent the bony growth which obstructs the mobility of the joint. The anti-inflammatory properties of the steroids also help to bring about gratifying symptomatic relief to the patient.

Osteoarthritis is by far the most common type of arthritic disease seen in old age. It involves mostly the large weight-bearing joints, such as the feet, knees, hips and lower back. It is characterized by primary degeneration of the joint cartilage with later involvement of the bone of the joint margin. There is simul-

taneous bone destruction and rebuilding, so that little spurs of bone jut out into the joint cavities and block them (26). Although osteoarthritis does not belong to the so-called "collagen diseases," cortisone and pregnenolone have been tried therapeutically in patients suffering from this condition. In the patients treated the changes were confined almost entirely to the periarticular structures and to the mental attitude (27). Although there was some loss of pain in the periarticular region, a decrease in the swelling and an increase in the joint mobility, there was no alteration in the joint lesion itself (27). The corticosteroids, therefore, induced a remission but no healing of the osteoarthritis. The cortical hormones may prove of value not only therapeutically, but experimentally in geriatrics. Solez (25) in discussing the theory that each stressful situation during life induces adrenal cortical response, points out that this hormone elaboration, in order to cope with the situation, temporarily alters the body physiology. He believes that each cortical hormone release, although temporary in its action, leaves its mark on the body tissues. Therefore the clinical picture of a geriatric patient is, partly at least, the sum total of the stress responses which he has experienced. Observations on the role of the corticosteroids in the production of arteriosclerosis, hypertension, osteoporosis and other diseases commonly seen in the aged may be the guideposts to the secrets of the aging process.

FURTHER USES OF THE STEROIDS

The use of steroid combinations or supplementary steroid treatment has many more applications than those already mentioned. Investigations of the uses of steroids in arteriosclerosis have proved fruitful. Arteriosclerosis in all of its forms is one of the most important considerations in the study of the aging process. It ranks first as a cause of death in the United States (28). It is seen in all age groups, but it is most common in the middle aged and elderly. The main result of these arteriopathies is a decrease in the amount of blood which the arteries can transport. Reduction of the blood flow with the following ischemia causes atrophy, malfunction and death of the tissues of the body. Many of the changes seen in aged patients are due to decreased blood supply to the area of the change. Arteriosclerosis, of which the more common clinical aspects are known as atherosclerosis, is reversible in experimental animals and humans. The etiology of the disease is still uncertain, but it is known to be related to high blood cholesterol levels and poor lipid metabolism. Therapy in these patients is complex, and includes dietary management and the use of lipotropic agents. Steroids, especially androgens and estrogens have been shown to be of great value in reversing the atherosclerosis in animals (29, 30). These hormones administered in daily doses increase of the phospholipid-cholesterol level, thereby improving the clinical picture of the atherosclerotic patient (28). Best results have been achieved with estrogen-androgen combinations, in patients over 50 years old. According to Morrison, the combination of dietary, lipotropic and hormonal therapy has resulted in reduction of the mortality rate in patients with coronary atherosclerosis, disappearance or decrease in anginal symptoms and a general feeling of well-being (28).

That the steroids augment each other as well as other hormones has been

previously pointed out and is again demonstrated by the fact that testosterone is of value in treating Addison's disease. It appears to augment the effects of the corticosteroids (22). In certain menopausal thyroid disorders, estrogens may augment the action of the thyroid hormone (31).

CONCLUSIONS

In surveying the literature of the use of steroids in geriatric therapy, certain facts stand out as principles to be observed. First of all, one should keep in mind the far-reaching effect of steroids on the various body tissues. Administration of a specific hormone may alter the metabolism and function of more than one organ and produce many effects other than the ones desired. It is wise, therefore, to evaluate the possible results of steroid therapy in the light of the patient's ability to adapt to the changes.

Secondly, aged tissue is less responsive to hormonal action than is younger tissue. This may mean that larger doses and more time will be required to produce the desired results. Fortunately, in aged patients sex steroids can be administered in large doses without fear of inhibition of spermatogenesis or oogenesis.

Most of the endocrine dysfunctions in elderly people are polyglandular in nature. No one steroid can, in such cases, alleviate the disorder completely. Combinations of hormones may substitute for the pluriglandular deficiency, counteract the untoward effects of each other, and aid each other by a synergistic effect. A third point might, therefore, be made that multihormone therapy designed for the needs of the individual patient and approaching as nearly as possible normal blood concentrations may prove the most effective way to utilize the steroids.

Lastly, it must be remembered that geriatrics points up more than any other branch of medicine the fact that therapy must be designed and constantly modified to the requirements of the individual patient. Each geriatric patient represents a completely different problem, the results of all the stresses, injuries, and nutritional and functional deficits he has experienced in his lifetime. "Tailor made" therapy thus brings effective results psychologically as well as physiologically. It is gratifying to the geriatrician as well as to the patient, who frequently needs a sympathetic ear as much as medication.

The present results with steroid therapy in geriatrics are astonishing; their future possibilities stagger the imagination. Steroids especially designed to produce a certain effect with no side-actions would be widely acclaimed. Radioactive steroids for therapy and clinical investigation may soon show us some of the secrets of cellular hormone utilization. With their abilities to reverse the body's metabolic age the steroid hormones make geriatrics one of the most important and satisfying fields in the practice of medicine.

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EVALUATION OF AN AMPHETAMINE-BARBITURATE COMBINATION IN THE SUPPORTIVE TREATMENT OF THE AGED

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In recent years it has become a paradoxical fact that medical achievement has increased rather than lessened one of our major health problems. Advances in surgical and medical techniques and the new knowledge resulting from biologic and pharmaceutical research have so extended the average life span than an ever-increasing segment of our population is faced with the difficult mental and physical adjustments accompanying old age. It has been estimated (1) that by 1960, 15.5 million Americans will be 65 or older. In 1940, only 9 million had attained this age.

The aims of medicine have been focused, for the most part, on the improvement and maintenance of health in youth and middle age; most of the skills acquired are logical developments of these aims. Not infrequently, however, techniques which are of benefit for most patients are of less value in the treatment of the aged, for the medical requirements of the elderly are not quite the same as those of younger patients. In addition to biologic changes, old people undergo mental modifications which often result in profound alterations in personality.

The older personality is characterized by a lowered drive, and feelings of insecurity and inadequacy (2–5) which frequently cause or aggravate the patient's complaints. One of the primary purposes of any therapy directed toward the aged must be the alleviation of undesirable mental states.

Several investigators (6, 7, 8) have found amphetamine helpful in relieving depression and restoring mental alertness in the elderly, and others (9, 10) have successfully used barbiturates to provide relief from tension and anxiety. It has been the author's experience, however, that these drugs, although occasionally helpful, are of very limited value in the treatment of the elderly. Amphetamines at times unduly increase nervousness and excitability; barbiturates often depress rather than sedate.

Since Myerson (11) first called attention to the reciprocal pharmacologic effect of amphetamine-barbiturate combinations, a medication incorporating *d*-amphetamine sulfate and amobarbital[1] has been favorably reported for the treatment of depression (12, 13, 14). In 1950, Grahn (14) successfully treated 85 depressed patients with the combination, several of whom were middle-aged and older.

In view of these reports it was decided to make a controlled study to see what effect, if any, this medication would have on the mental and behavior patterns

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[1] Dexamyl, Trademark, Smith, Kline & French Laboratories, Philadelphia, Pa.

of 52 very old people who are residents of the Masonic Home for the Aged in Guthrie, Oklahoma.

In addition to testing the efficacy of the medication it was felt that a perhaps more interesting result of the study would be the highlighting of some problems peculiar to the treatment of the aged. These problems are presented in the discussion at the end of this paper.

SUBJECTS

The Masonic Home for the Aged has a population of 100 old people who vary in health from those who are up and about, to those who are quite ill and bedridden. The average length of stay is ten years. Admittance to the home is limited to persons from families of third degree Masons, and the Blue Lodge or Eastern Star members.

The 52 patients chosen for this study represent a particularly challenging group. Products of a middle-class to upper-middle-class environment, they had been accustomed to a more than average amount of financial security, independence and community esteem. Consequently, one might assume that their problems of adjustment to institutional life would be marked. For many of these people, normal environmental adjustments were made more difficult by grief over the death of loved ones, loneliness following the moving away of older children, and depression resulting from the discovery of, or more advanced development of incapacitating disease. All of them exhibited in varying degrees the bewilderment and anxiety so often seen in the aged, and it was felt that the treatment of these people provided a singularly difficult test for the medication.

The patients ranged in age from 76 to 92 years. The average age of those in whom results are reported was 76.5 years. The majority of these (78 per cent) were women, but since there were no differences in reaction attributable to a difference in sex, the results for men and women have not been analyzed separately.

METHOD

The study was conducted for one year and includes four evaluations of the drug. Each evaluation was made at the end of a three-month period.

In order to make the study as objective as possible, placebos—identical in appearance to the drug—were alternated with the active medication. With few exceptions (noted under "Results"), the patients who were first given the active medication were then switched to the placebo; conversely, those who received the placebo first were then switched to the active drug. In this way each patient served as his own control.

Both medications were coded, and the code—which was kept at the Oklahoma Medical Research Institute in Oklahoma City—was not known to the author or his staff. At no time did the patient or physician know what medication was being given. The dose of Dexamyl (1 tablet[2] three times daily after meals) re-

[2] Each tablet contains 5 mg. of *d*-amphetamine sulfate and 32 mg. (½ grain) of amobarbital.

mained constant. All patients were given other medication as needed; from time to time most of them received salicylates, vitamins and mild cathartics.

The patients were free to drop from the study at any time, and the potential value of the drug was not stressed. Their reaction to the medication was shown by spontaneous changes in mental and physical activity.

Patient response was evaluated by the Gardner Behavior Chart,[3] a reliable, comparatively objective device that is of particular value for the periodic analysis of the mental and physical patterns in continual-care patients. In addition to general response, the following characteristics were observed: personal appearance, sleep, appetite, sociability, activity control, temper control and self entertainment. These aspects of each patient's behavior were observed at intervals which were never more than two weeks apart.

Although the active drug seemed remarkably effective in a few patients, the possibility of the patient's overwillingness to please, and the probable subjective differences in the observer's interpretations weighed against our classifying any of the results as excellent.

RESULTS

First six months: Of the 52 patients who started the study, 28 dropped out before the end of the first six months. Since it was felt that at least six months (three months on each medication) was necessary to obtain a significant evaluation of the drug, these patients are not included in the study. They, together with those who dropped out in the second six months, will be discussed later.

Two deaths occurred during this time. One woman of 84 died of a cerebral accident; another aged 86 died from a cardiac condition. Neither of these deaths was in any way attributable to the medication. Considering the unusually advanced age of the group, the difficulties in managing such people, and the ostensibly relaxed manner in which the study was conducted, the number dropping out was about what one would anticipate.

In this first six-month period, the administration of the amphetamine-amobarbital combination resulted in improvement in 18 of 26 trials, and in no improvement in 7 trials. In 1 instance the patient was made worse. In only 3 of 18 trials was the placebo credited with having a beneficial effect. The placebo resulted in no improvement in 9 trials, and in 6 instances patients seemed worse.

Second six months: Five very weak and debilitated patients were not permitted to continue the study for the second six months. Two patients—a 76-year-old man suffering from uremia, and an 80-year-old woman suffering from cancer of the uterus—died before the six months were completed. Nineteen patients (2 of them, new) began this final half of the study and 9 patients voluntarily discontinued the medication before the results could be evaluated. Of the 10 trials of the active medication that were completed in this period, 8 resulted in a beneficial effect and 2 did not. Of the 10 placebo trials, 5 seemed to result in fair improvement and 3 in no improvement; 2 patients were made worse.

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Complete results

The total results of the one-year study on the patients who were under medication for six months or longer are summarized as follows:

Medication	No. of trials	Results			
		Good improvement	Fair improvement	No improvement	Made worse
Dexamyl	36	25	1	9	1
Placebo	28	0	8	12	8

Although the number of cases is small and the quantitative results might be modified in a larger series, it does appear from the data available that there was a decided qualitative difference in the response of these patients.

In the first three months, only 3 of 11 patients improved while receiving the placebo; 9 of the same 11 improved while receiving the active drug. When 7 of these were started on the placebo for the second time, none of them improved. Again, none of the 7 patients who improved while taking the active drug in the first period showed any improvement when given the placebo. These findings were consistently observed during the entire course of the study.

The most common beneficial effect of the drug was the alleviation of depression and an increase in sociability and activity resulting in improved personal appearance and ability for self entertainment. The patient who was made worse by the drug suffered a loss of appetite and a consequent reduction in weight. In view of the patient's age and physical condition, this offset any other improvement.

Incomplete results

Of the 28 patients who did not complete the first six months of the study, 16 discontinued the active drug and 12 discontinued the placebo.

The 16 patients who dropped the active drug complained of one or more of the following symptoms: gastrointestinal distress (9 complaints, all from arthritics), backache (1 complaint; patient had prostate trouble), sleeplessness (5 complaints), nervousness (3 complaints), and hypertension (1 complaint). Two patients did not like the medication.

Of the 12 who discontinued the placebo, 8 complained of gastrointestinal distress (all were anemic arthritics), 2 were too disabled to take the medication faithfully, and 4 gave no reason for discontinuing.

Of the 7 patients who did not complete the last six months of the study, 5 discontinued the active drug, and 2 discontinued the placebo. Of the 5 patients who discontinued the active drug, 2 complained of gastrointestinal distress, 2 of weight loss and one of increased blood pressure. Of the 2 patients who discontined the placebo, one was discouraged over lack of response, and 1 complained of increased blood pressure.

Side effects

Of the 52 patients observed, 10 experienced side effects that could be definitely attributed to the drug. These were: sleeplessness and nervousness (7 patients); and weight loss (3 patients).

DISCUSSION

The fact that the active drug and the placebo were discontinued by about the same number of people and, in most cases, for the same reasons, illustrates one of the major difficulties in treating the aged. Old people with little hope for the future and less interest in the present, lack many of the motivations for improvement that operate in younger patients. Actually, the medication seemed to be helping a few of the people who dropped from the study and, curiously enough, it seemed that this was the underlying reason for their discontinuing the medication. There are some old people who are afraid of health, who view their disabilities as something like accomplishments entitling them to greater prestige, attention and affection; and they tacitly resist anything that may threaten to deprive them of the bleak benefits of ill health. Obviously, no drug in itself can have a more than transient value for these patients.

In this regard, it might be well to point out that any person's ability to adjust does not depend alone on the number of years he has lived, but rather on the way he has lived his years. The ideal treatment of age, then, should begin in youth. Drugs cannot be expected to supply the answer to deep-seated personality problems—but they can help. The results of this study suggest that the *d*-amphetamine-amobarbital combination is of decided value in the supportive treatment of depressed, but comparatively well-adjusted old people.

There is reason to believe that there are certain personality differences between institutionalized and non-institutionalized old people. Davidson and Kuglow (4) report that the institutionalized aged have a lower energy output, greater rigidity of personality and less emotional responsiveness than non-institutionalized people of the same age. Although the results achieved in this study are not applicable to any but the patients observed, it seems possible that the medication could be at least equally effective in treating non-institutionalized old people of less advanced years who are so frequently seen in the physician's office.

SUMMARY AND CONCLUSION

A one-year controlled study is reported of a *d*-amphetamine sulfate-amobarbital combination (Dexamyl) in the treatment of 52 very old residents of the Masonic Home for the Aged in Guthrie, Oklahoma. Four three-month evaluations of the drug were made. Placebos were alternated with the active medication, and both drugs were coded; at no time did the author or the patients know which medication was being given. The patients were free to drop from the study at any time. Response to the medication was evaluated by the Gardner Behavior Chart.

The active drug resulted in improvement in 26 of 36 trials; in only 8 of 28 trials was the placebo credited with having a beneficial effect.

Side effects attributable to the drug were observed in 10 of the 52 patients. Seven complained of sleeplessness and nervousness, 3 of weight loss.

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PULMONARY EMPHYSEMA TREATED BY INTERMITTENT POSITIVE PRESSURE BREATHING

A Clinical Study*

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Emphysema and its complications are evoking more and more medical interest. Expectation of life at birth among workers in the United States in 1952 reached sixty-eight and a half years. This represents a gain of slightly more than four years in the past decade and of about twenty-two years since 1912 (1). With advancing age, more complications of diseases develop and become clinical problems—as in diabetes, for example (2).

Much medical interest is centered in these groups of diseases. The background for this work was reviewed under the title "Pulmonary Insufficiency" by Baldwin, Cournand and Richards (3). The approach has been greatly broadened by the pulmonary function studies of Cournand and Richards, of Pinner and Zavod, of George Wright and of Comroe, and by the early interest in therapy of Barach *et al.* (4, 5) of Gordon *et al.* (6), of Segal and Dulfano (7) and others.

Intermittent positive pressure breathing has been used with increasing frequency in recent months in the treatment of pulmonary emphysema and its concomitant diseases. The literature on this subject is not extensive. The reviews of clinical data recently published by Smart *et al.* (8), Motley (9), and Motley and Tomashefski (10) have summarized the changes in pulmonary function which occur after such therapy has been administered. The idea behind the application of intermittent positive pressure breathing to emphysema and other chronic lung disease is that it increases the efficiency of aeration of the lung, promotes bronchial drainage and, if a bronchodilator such as a nebulized aerosol is added, helps correct that portion of the bronchial narrowing due to reversible bronchospasm.

MATERIAL AND METHODS

Our own use of this method of treatment goes back about eighteen months. In the beginning some of the patients may have been poorly chosen, and others, for various reasons, have not continued the prescribed treatment. The 35 patients we are considering here have been followed for periods of from two weeks to several months. They are private patients, who, on the whole, have been very

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TABLE 1

Symptomatic Improvement

Symptoms	No. of Patients	Improved		Unimproved	
		No.	%	No.	%
Dyspnea	31	24	78	7	22
Cough	32	22	69	10	31
Sputum	30	20	67	10	33

cooperative, have been under close observation and have had a good follow-up. All the adjunctive treatments for pulmonary emphysema and its allied conditions were used when indicated in each patient. We therefore have no controls as such.

We are not discussing the emergency use of positive pressure breathing for the relief of pulmonary edema, whatever the cause.

Our method of administering intermittent positive pressure has been given in detail by Motley *et al.* (11). One hundred per cent oxygen is inhaled through a Bennett[1] valve, type TV-2P, which allows oxygen flow into the lungs under regulated inspiratory positive pressure of up to 20 cm. of water. As inspiration is completed, the valve cycles, the oxygen stream is shut off, and expiration is entirely passive. The patient chooses his own rate and depth of breathing. A mask is used by us for all patients. A bronchodilator aerosol, isopropylarterenol (NNR) (Isuprel®), is nebulized into the oxygen stream in most of the patients. Other bronchodilators have also been employed but this has been the most satisfactory for general use.

Of the 35 patients considered here, 2 have had two courses of treatment, making a total of 37 observations. Pulmonary emphysema was found in 27 cases. Of these, 11 had chronic recurrent bronchial asthma, 2 had advanced silicosis, and 2 had bronchiectasis concurrent with pulmonary emphysema. The other diagnoses, listed in the order of their numerical importance, were as follows: chronic bronchitis, 5 cases; arteriosclerotic heart disease, 2 cases; pulmonary fibrosis, 1 case; peripheral vascular disease, 1 case; and uremia, 1 case.

OBSERVATIONS

Table 1 shows the improvement noted in these patients. The three most outstanding complaints, as expected, were dyspnea, cough and sputum. Of the 31 patients who complained of dyspnea, 24 (78 per cent) showed moderate to great improvement. It is of interest that this improvement was usually first noted within three weeks from the beginning of therapy. However, in some cases, it required as long as six months for the improvement to become maximal and reach a plateau. The same time range applied to the improvement in cough and sputum. Usually some change was noted within the first three weeks, although here again, it occasionally required four to six months for maximal improvement to become noticeable.

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TABLE 2

Improvement in Patients with Dyspnea

Diagnosis	No. of Patients	Improved		Unimproved	
		No.	%	No.	%
Pulmonary emphysema	23	16	70	7	30
Asthma	10	7	70	3	30
Bronchitis	5	3	60	2	40

TABLE 3

Improvement in Patients with Cough

Diagnosis	No. of Patients	Improved		Unimproved	
		No.	%	No.	%
Pulmonary emphysema	22	16	73	6	27
Asthma	10	6	60	4	40
Bronchitis	5	3	60	2	40

TABLE 4

Improvement in Patients with Sputum

Diagnosis	No. of Patients	Improved		Unimproved	
		No.	%	No.	%
Pulmonary emphysema	23	16	70	7	30
Asthma	10	7	70	3	30
Bronchitis	5	3	60	2	40

The improvements in symptomatology are listed, according to diagnosis, in Tables 2, 3 and 4. These figures are self-explanatory.

In addition to improvement in cough, sputum and dyspnea, all of the improved patients stated that they noted an increased ease of breathing, that it was easier to get air in and out, and that it was easier to take a deep breath. Most of them also noticed a decrease in fatigue; a moderate number had increased appetite and felt generally better. Many slept better.

An attempt was made to decide in advance those patients who might be improved and those who might not be improved. This was impossible. The history, including the duration of the disease and the presence or absence of asthma or chronic bronchial infection, was of no value. In each category, as many patients improved as failed to improve. Physical signs were generally useless. The presence or absence of rales in the chest, the intensity of the breath sounds, and the presence or absence of a barrel chest likewise had no prognostic significance. The only factor which was found to have some bearing on the response to intermittent positive pressure breathing was high-pitched, sibilant expiratory rales. All of the patients with this finding were found in the improved column in all symptomatic

groups. Only one of the patients who failed to improve showed this physical finding. However, the reverse was not true. Many patients who were listed as improved never had expiratory sibilant rales.

The fluoroscopic findings also failed to provide a prognostic clue. The absolute level of the diaphragms and their relative mobility were investigated, and were not of prognostic value. As many patients with flat immobile diaphragms improved, as with rounded mobile ones. The presence or absence of increased pulmonary markings was likewise not correlated with either improvement or lack of it. The presence or absence of accentuation of the pulmonary artery and the appearance of right ventricular hypertrophy also were investigated, and were not found helpful.

It is interesting that, although only 2 patients with silicosis were treated in this series, both of them had advanced roentgenologic disease with severe symptoms, and both improved very markedly and rapidly. One of them has been able to maintain his improvement for a period of three months after discontinuing treatment. The other patient is still undergoing treatment.

Typical Cases

T. H. was a man aged 60. At the outset he could walk only a few steps. Now he walks ten blocks with only slight discomfort, much further improvement having been noted in the past couple of weeks. He stated "I never thought I could ever again feel as well."

In January 1951, the patient reported that for a long time he had had shortness of breath on mild exertion—"can't walk more than half a block on the level before stopping for breath." He was raising about two ounces of sputum each morning, and about four ounces during the next twenty-four hours. Bronchoscopy revealed a marked redundant mucous membrane, involving almost the entire bronchial tree. In March 1951, a number of large emphysematous blebs were removed from his right chest, with denervation of his right bronchial tree. On the operating table the lung expanded, filling the space occupied previously by these large blebs, and he showed almost immediate improvement in respiration. In a few weeks he went home, and had symptomatic care and treatment from his local physician. He had so much relief, however, that he was impatient with his condition, though it was much better, and wanted "an operation on his other side." In November 1952, he was given Bennett valve therapy. In two weeks his walking was distinctly improved. He had "a lot more wind" after each treatment, but he gradually lost this during the day. Each morning he was conscious of shortness of breath again. Fluoroscopically, however, his diaphragmatic excursion slowly improved. By February 1953, three months later, he "walked up fourteen steps without any difficulty at all." In March this improvement was more marked. At that time he went home (upstate), taking a Bennett valve with him. He was seen six weeks later and improvement had continued. He had begun to walk up small hills with impunity.

E. R. was a man aged 58, who was first seen in May 1941 because of chronic nonproductive cough and some wheezing. He had mild emphysema and some secondary bronchial infection. Bronchograms and bronchoscopy showed no evidence of bronchiectasis. He was seen again in 1948 for a few weeks for a respiratory infection which cleared. In September 1952 he came in because of productive cough, shortness of breath, inability to lie down at night, and interrupted sleep because of frequent coughing. This had been gradually increasing for at least two years. In November 1952 he received Bennett valve treatment, with a bronchodilator. Two weeks later he reported that he slept all night for the first time in years—no coughing, used only one pillow, didn't wake—and he felt markedly improved. This improvement continued.

It was interrupted by a respiratory infection which, however, cleared promptly. At present, he does very well in the daytime, but by night he gets a little tired. He coughs only slightly and has very little sputum. (He finally stopped smoking completely, and his cough disappeared.) He says he has a lot more strength, breathes much better, and has "more wind" than he had before. He has "good second wind." He used to have to stop at the end of about two blocks; now he can keep walking if he doesn't go too fast, and has not reached a limit as to the distance he can go.

S. I. was a 71-year-old man, first seen in February 1953. He said he had been coughing for the previous two years, and had sputum every day. He was short of breath and had a hard time breathing when he walked around. Other physicians during this period had given only very temporary relief. The patient was given Bennett valve treatment. Within two weeks he was coughing less, sleeping better, had less dyspnea, no wheezing and no sputum. By March he volunteered that "I can beat you running." By April he said he was still improving. His pulmonary ventilatory function tests did not show any marked difference. He said he felt "peppier," was much more lively, slept better, and was working.

We have had this experience several times with pulmonary function tests by the Warring method. The tests show very little difference, but the patients are obviously very much improved clinically. These methods measure mass movements of air but may not be sufficiently sensitive to measure significant differences in oxygen exchange.

COMMENT

Our results in cases of chronic pulmonary disease treated by intermittent positive pressure breathing, plus other adequate measures, show that approximately two thirds of our patients experience substantial improvement. This agrees with previously published reports (8, 9, 10). It thus appears that intermittent positive pressure breathing is valuable therapy in pulmonary emphysema. It provides marked relief from symptoms, makes the patient more comfortable, frequently allows him to pursue a gainful occupation, and removes him from the list of economic dependents. This is in contrast to our previous experience with some of these same patients when they were treated with other methods but without intermittent positive pressure oxygen therapy. Oxygen alone had no such value. Moreover, our experience with other patients of this type helps to verify our conclusion that the intermittent positive pressure breathing is the decisive factor.

Only simple pulmonary function studies have been carried out by us in our patients. Motley and Tomashefski (10) have covered the field competently and have presented an evaluation of patients before and after intermittent positive pressure breathing treatment, by objective physiologic measurements. Of these, they found that the maximum breathing capacity was the most significant, and the simplest measurement which could be correlated with clinical observations of improvement. There was usually no change in the residual volume, or in the ratio of the residual volume to the total capacity, except in an occasional case. Physiologic measurements reveal a more uniform alveolar aeration following intermittent positive pressure breathing (12).

SUMMARY

This study covers 37 patient observations in which intermittent positive pressure breathing was used for a sufficient length of time to allow more than

temporary results. Our findings, which confirm previously published reports, show that improvement occurs in more than two thirds of patients with pulmonary emphysema and with other chronic lung diseases involving problems of bronchial drainage.

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TREATMENT OF HYPERTENSION IN THE ELDERLY PATIENT

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CLASSIFICATION

From the standpoint of practical therapeutics, four kinds of hypertension in the elderly should be distinguished:

1. Arteriosclerotic, associated with arteriosclerosis of the large vessels.

This is manifested by a wide pulse pressure and usually has a benign prognosis. Treatment is symptomatic only: salt restriction or mild depressor agents often dramatically relieve symptoms without great effect on the blood pressure.

2. "Malignant" hypertension as manifested by rapidly rising blood pressure, papilledema, retinal hemorrhages and exudates, and renal damage.

This complication of hypertensive disease is rare in the elderly. As pointed out by Perera (1), it may be the clue to a Goldblatt type of hypertension, with one kidney involved by an arteriosclerotic plaque or, as we have seen recently, by a slowly progressing ureteral obstruction such as that caused by carcinoma or irradiation fibrosis.

3. "Essential" hypertension with onset after the age of 50.

It is most unusual, as Perera has emphasized, for hypertension to begin after the age of 40. It is probable that hypertension with so late an inception will remain benign. This type is easily confused with the arteriosclerotic variety and is to be identified by a relatively smaller pulse pressure and a diastolic blood pressure usually over 110. It needs no treatment, unless for symptoms or for vascular complications.

4. "Essential" hypertension with onset in middle life and extending into the later years.

When this variety is identified by a specific history, the prognosis for the individual is largely based upon the magnitude of vascular disease in the heart, (by teleoroentgenogram and electrocardiogram), kidneys (urine albumin, phenolsulfonphthalein, urea or creatinine clearance), and cerebral vessels (history or signs of "strokes," vasospastic episodes, or diffuse cerebral degeneration). If these findings are normal, and particularly if the patient is an obese female, the prognosis appears excellent, almost regardless of the high blood pressure. However, in cases with sustained high pressures, a cerebral hemorrhage may occur without warning. If any complications are present, treatment is justified, but the choice of drug will depend upon the age and general status of the patient. Drastic measures are to be avoided.

TREATMENT

Treatment may take several forms such as *dietary, surgical or pharmaceutical.* Salt should be restricted to the 200 mg. level for a trial period of three months,

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during which blood pressure, salt excretion and symptomatology are checked on fortnightly visits to the physician. If improvement does not occur at the end of this time, the diet may be gradually abandoned. If the blood pressure falls or symptoms such as headache, dizziness, angina, dyspnea or edema are relieved, the diet is gradually modified upward to the 500–800 mg. level. The usual experience of a patient on the low-salt diet is that lassitude and weight loss occur during a period of from three to four weeks, followed by stabilization and an improved sense of well-being. Consequently, at the end of the trial period, many patients refuse to return to a free salt intake, because they feel better without it. Unfortunately, reduction in blood pressure of significant degree is infrequently observed, but the symptomatic relief and the alleviation or postponement of cardiac symptoms seems to justify this management in most elderly hypertensive subjects. In my experience, cases of excessive sodium loss associated with the "low-salt syndrome" are rarely encountered, although elderly patients with renal function less than 50 per cent of normal may occasionally get into difficulty during such a rigid salt restriction. If further measures, such as diuretics or resins are prescribed for elderly hypertensive individuals without edema, serious derangements may occur.

Sympathectomy has in general been considered inapplicable to the elderly hypertensive patient but, in my opinion, certain cases clearly benefit. The expectation of significant reduction in blood pressure is at least as good as in the younger subjects (2) and significant symptomatic relief may also occur. In most instances, less drastic methods will prove satisfactory in the elderly, in whom our therapeutic objective should not be normalization of the blood pressure but rather relief of symptoms and reduction to reasonable levels, in order to avoid or lessen the complications of the disease.

Drug treatment of hypertensive disease is still in the exploratory stage. Table 1 illustrates the present choice of therapeutic agents. *Rauwolfia serpentina* derivatives are only mildly effective but some of their side effects may be particularly useful in the management of the elderly (3). *Hydrazinophthalazine hydrochloride* (*hydralazine*) (*Apresoline*) is an excitatory drug which greatly increases the circulation (4). It should be employed cautiously in cardiac patients. *Hexamethonium chloride* (5) and *Veratrum viride* (*Protoveratrine*) derivatives (6) are potent and should be used with great caution in the elderly.

Since hypertensive disease varies widely, an attempt will now be made to relate the treatment to various types of hypertensive disease in the elderly, as follows:

1. *Blood pressure usually below 200 systolic; no complications*
   No treatment necessary.
2. *Blood pressure usually over 200 systolic; no complications*
   Treatment here is elective, depending upon the patient's age and cooperation. These individuals run the risk of cerebral hemorrhage at any time, but if in good condition and cooperative, they deserve a trial of therapy, in this order: 1) Sodium restriction, 2) Rauwolfia, 3) Apresoline.

TABLE 1

NEWER DRUGS IN THE CHRONIC TREATMENT OF HYPERTENSION

Generic Name	*Rauwolfia serpentina*	1-Hydrazinophthalazine hydrochloride (hydralazine)	Hexamethonium chloride*	*Veratrum viride*
Trade Name	Raudixin (Squibb)	Apresoline hydrochloride (Ciba)	Methium (Chilcott); Hexamethon (Burroughs, Wellcome) etc.	Protoveratrine (Lilly)
Dose	50–100 mg., 2–3 x daily	10–200 mg., 3–4 x daily	125–750 mg., t.i.d., p.c. & h.s.	0.75–1.5 mg., p.c. (breakfast) & h.s.
Mode of action	"Central" hypothalamic?	Direct vasodilatation	Ganglionic blockade	Afferent stimulation of vasomotor centers
Objective in hypertension	Moderate sustained BP reduction in mild cases	Moderate diurnal BP reduction in some cases	Diurnal reduction of orthostatic BP; less effect on recumbent BP	Daily reduction (6–8 hrs.) in erect or recumbent BP
Side effects:				
a) Useful	Decrease in: pulse, anxiety Increase in: weight, bowel movements	Cardiovascular stimulation; increased renal blood flow	Decreased tendency for vomiting	Decreased pulse, and improved cardiac efficiency
b) Minor, unpleasant	Fatigue, nasal stuffiness	Headache, GI symptoms, tachycardia	Cycloplegia, dry mouth, constipation, orthostatic hypotension	Nausea, vomiting, extreme hypotension
c) Serious	—	Drug fever with arthralgia, etc.	Ileus, bladder paralysis, increased azotemia	Heart block
d) Preventive measures	—	Avoid, in patients with drug sensitivity	Saline laxative daily; no drug, if constipated 24 hrs.	Omit during digitalization
General contraindications	Fatigue states; obesity	Angina; ?heart failure	Prostatic hypertrophy; cerebral arteriosclerosis; impending uremia	Cerebral arteriosclerosis

* May be given s.c. 2–3 times daily; may be combined with hydralazine.

3. *Blood pressure moderately elevated; symptoms or complications present*
   a. *Angina.* Salt restriction is frequently beneficial and, together with the accepted coronary vasodilators, is the treatment of first choice. In our hands the sedative and bradycardiac effects of Rauwolfia are sometimes helpful in managing angina pectoris. The tendency to obesity must be controlled, however. Oral hexamethonium is to be tried cautiously in order to avoid steep falls in blood pressure with the risk of precipitating coronary thrombosis. Moderate reduction in blood pressure often seems to relieve pain. Apresoline is contraindicated. Protoveratrine may be helpful.
   b. *Congestive failure.* Conventional methods should be tried first, with emphasis on salt restriction (200-mg. sodium diet). If the blood pressure remains high and dyspnea or edema recur, hexamethonium should be used to control the daytime (ambulatory) blood pressure. Protoveratrine, if necessary, should be taken nightly for control of paroxysmal dyspnea. Hexamethonium must be used cautiously, as it may produce cumulative toxic effects in the face of the renal insufficiency which commonly accompanies congestive failure. Rauwolfia may help, especially if tachycardia is persistent, but it cannot be expected to lower the blood pressure markedly in most cases. Apresoline is probably contraindicated.
   c. *Cerebral thrombosis.* Apresoline is theoretically the drug which is the most likely to improve cerebral blood flow. Despite this, I have seen thromboses occur in 3 patients taking Apresoline, without significant reduction in blood pressure. Measurements of the effect of the drug on cerebral resistance show only slight improvement (4). Consequently the choice of Apresoline for the treatment of cerebral thrombosis is not made with great conviction. Hexamethonium and Protoveratrine may lower the blood pressure too sharply and extend the thrombosis. Rauwolfia is probably not effective. Since reductions in pressure without concomitant cerebral vasodilation in an elderly person are likely to produce adverse effects, patients who have had thrombotic accidents as the only complication of hypertension should not be treated wtih depressor drugs.
   d. *Cerebral hemorrhage.* The dramatic manifestations of this complication theoretically call for acute reduction in blood pressure. In practice, however, control of blood pressure during such an episode is difficult. Hexamethonium has acute effects but when the intracranial pressure is increased from bleeding, patients are extremely sensitive and may respond with severe hypotension. The drug should be given at a rate of 0.5 mg. per minute intravenously, with the patient in the sitting position and the blood pressure recorded every thirty seconds. Arfonad, a new vasodepressor, may prove more useful in such emergencies, as its effects are more transient and hence more controllable (7). When a patient presents himself with the residual effects of an old cerebral hemorrhage, a difficult therapeutic decision has to be made. In general, only symptomatic treatment is advised, because hypotensive therapy may precipitate a thrombosis; on the other hand, lack of hypotensive therapy may result in a hemorrhage. If the blood

* May be given s.c. 2-3 times daily; may be combined with hydralazine.

pressure is usually over 200, moderate measures of treatment, such as salt restriction, Rauwolfia, Apresoline or even hexamethonium and Protoveratrine may be tried, provided the patient's general condition is good. Otherwise, it is best to avoid hypotensive drugs.

e. Hypertensive encephalopathy. By this term is meant the acute focal or generalized neurologic disturbances produced by severe hypertension in the absence of uremia or of chronic cerebral arteriosclerosis. When the latter complications can be ruled out, vigorous therapy is often dramatically effective in restoring consciousness and clearing residual neurologic symptoms. Hexamethonium should be given intravenously *very slowly*, as described previously, until the blood pressure is lowered to 170–180 systolic.

f. Renal complications. Azotemia contraindicates almost all definitive drug therapy, because the prognosis is nearly hopeless anyway and vasodepression may lead to rapid progression of the uremia. There are two exceptions: 1) When the azotemia is pre-renal (*i.e.*, cardiac, or due to dehydration) and responds to appropriate treatment, and 2) when other symptoms demand attention regardless of the renal status (*i.e.*, convulsions, impending blindness from retinopathy, or refractory left ventricular failure). In the former instance hexamethonium should be very cautiously administered by subcutaneous injection beginning at 5 mg. every four to six hours and increasing by 5 mg. per dose until the blood pressure is lowered to a reasonable level. During this time, daily creatinine or blood urea determinations will indicate whether the uremia is improving or not. If not, treatment should be stopped immediately. Ileus, which may come on abruptly due to deficient renal removal of hexamethonium, is likewise a calculated risk in this situation. In the second instance, when uremia is clearly present, Protoveratrine or Apresoline is the treatment of choice. We favor the former in this situation, because the effect of Apresoline is often unpredictable. Considerable symptomatic relief may sometimes be achieved.

SUMMARY

The types of hypertension encountered in the elderly are described. Emphasis in treatment should be upon milder measures such as salt restriction, Rauwolfia derivatives and occasionally hydralazine. More vigorous methods such as sympathectomy, and the administration of hexamethonium chloride or Veratrum derivatives should only rarely be used.

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THE TREATMENT OF LAENNEC'S CIRRHOSIS OF THE LIVER

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Within recent years great advances have been made in our knowledge of the etiology and treatment of diseases of the liver. This presentation will be concerned with some considerations of the therapy of Laennec's cirrhosis of the liver. This term is used to define that complex of clinical, functional and pathologic changes which is most frequently associated with chronic alcoholism in this part of the world. Those hepatic cirrhoses which are associated with viral hepatitis, parasitic disease, syphilis, chronic congestive heart failure and prolonged biliary obstruction with infection will not be discussed.

In 1937 Patek reported that the administration of a nutritious diet with supplements of the vitamin-B complex favorably altered the clinical course of the disease in patients with edema, ascites, icterus and wasting (1). These observations have been confirmed and form the basis for the modern therapy of the disease (2, 3, 4). The rationale for this treatment was the high incidence of malnutrition, with associated evidences of vitamin deficiency states in these patients (1, 2). Since that time an abundance of evidence has accumulated to show that the liver depends for its functional and anatomic integrity upon a subtle balance of ingested foodstuffs (5). Although great strides have been made in understanding the importance of such substances as choline and methionine in the genesis of experimental nutritional liver disease, there are still many gaps in our knowledge of the development of Laennec's cirrhosis in man. For example, the stepwise evolution of the disease in man with concomitant clinical and histologic observations has not been documented in a single patient. Furthermore, the problem is more complex in man, in that the relatively pure deficiency states produced in experimental animals are not seen in human alcoholics. The studies in animals do offer working hypotheses for further investigations in man.

In former years, the diagnosis of Laennec's cirrhosis was usually made when the disease process was far advanced, with wasting, ascites, edema and icterus. With the progress in diagnostic techniques in this field, such as the newer liver function tests and needle biopsy, it is possible to diagnose the disease much earlier in its clinical course. It may be entirely subclinical and be discovered in the course of laparotomy for some unrelated complaint. There may be some or all of the following clinical findings noted in alcoholic subjects: apathy, confusion, dementia, malnutrition, peripheral neuropathy, glossitis, cheilosis, palpable liver, palpable spleen, "spider" angiomata, "liver" palms, icterus, and dilated lower abdominal veins. The symptoms may be those of alcohol withdrawal,

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abdominal pain, anorexia, nausea, vomiting and extreme weakness. The liver function tests may show minimal or moderate abnormalities.

At this stage of the disease, *dietary therapy* (C 350, P 100, F 125) is usually effective. Extra vitamins may be given if there are evidences of specific deficiency states or if alimentation is poor. In the latter case, their parenteral use may be preferred. When the patient has begun to eat, the response is usually favorable. There will be clearing of any sensorial disorders and icterus, with gain in strength and sense of well-being. The evidences of deficiency states will subside, although severe peripheral neuropathy may be very slow in improving. The results of liver function tests will improve and may return to normal. The time required for this reversal will vary, depending upon the severity of the presenting state. A period of one to three months may be needed to restore these patients. Certain physical findings, such as "liver" palms, palpable liver and spleen, "spider" angiomata, and dilated abdominal veins may persist after clinical recovery has occurred.

Liver biopsies in such patients may show varying degrees of fatty and periportal lymphocytic and fibrous tissue infiltration. The histologic picture is unpredictable (6). With clinical improvement, the main histologic change is disappearance of fat. There is no evidence that the administration of choline in addition to the nutritious diet has additional beneficial effects upon the liver (7, 8).

Laennec's cirrhosis may progress from the state described above to that in which there is marked wasting, ascites, edema and icterus. The liver function tests are more profoundly altered in such patients than in the foregoing group. Needle biopsy of the liver may reveal histologic patterns similar to those observed in the group of patients without ascites (6). There is no positive correlation between the severity of histologic change and either the clinical state of the patient or the results of the liver function tests. On the other hand, the poorer the clinical state, the lower the level of serum albumin and the higher the level of serum bilirubin (6). These patients are more gravely ill and present a much greater therapeutic challenge. Anorexia, abdominal pain and fullness as well as severe weakness are common. The same principles of dietary therapy obtain in these patients as in those previously described. When they cannot eat the diet offered, a liquid regimen may be designed, such as: one quart of milk, 4 to 6 raw eggs, 4 tablespoons of lactose, and 5 to 10 tablespoons of a protein hydrolysate or concentrate, flavored to the patient's taste. Additional small servings of food may be given as tolerated. The use of six to eight small feedings daily may be helpful. Great guile may be needed to induce these patients to eat. An attractive tray, good-tasting food, as well as all the other subtleties of expert nursing and dietetic care are needed. It is essential that their great nutritional needs be served. Patients who can eat nothing, including those in coma, should receive 20 per cent glucose in distilled water (2 liters per day) with added water-soluble vitamins, along with salt-poor human albumin. Early and dramatic improvement has been observed with the use of the latter material (9).

The presence of *ascites* with abdominal discomfort interferes with food intake. Abdominal paracentesis may be performed for comfort, in order to enable the

patient to eat. The retention of fluid may be treated more directly by: a) mercurial injections with or without ammonium chloride reinforcement (1); b) restriction of sodium intake (4), and c) exchange resins (10). The mercurials may be given twice weekly with 3 to 5 grams of ammonium chloride for reinforcement. In favorable instances brisk diuresis will occur and paracenteses may be spaced more widely. A diuretic response to mercurials is a good prognostic sign. Often diuresis is not seen early in the course of treatment but does occur later, as clinical improvement takes place. Since large amounts of potassium may be lost following mercurial injection, whether or not sodium and water diuresis has occurred, symptoms of potassium loss may appear and indeed hypokaliemia may develop (11). Care must be taken to replace potassium in such patients. Many gravely-ill patients may have reduced levels of serum sodium (12). These may return to normal with improvement.

The markedly positive sodium balance of these patients (13) has been treated by severe restriction of sodium intake, with consequent lessening of fluid retention (4). Although low-salt diets are effective in controlling fluid retention, they are difficult to prepare without compromising the taste and attractiveness of food. Since it is more important for the patient to eat well of a nutritious diet than to be concerned over the salt intake, a useful tool is the ammonium-potassium exchange resin. This compound, when fed, takes up sodium from the bowel and may be given to obviate rigid salt restriction in diets (10). It may be used along with mercurials. It is well to observe that frequently the management of fluid retention obscures the fact that the major problem is one of the diseased liver. The development of fluid retention is a physiologic consequence of the diseased liver and not a disease entity in itself.

Adjuncts to the dietary therapy just outlined have been employed. Oral brewers' yeast powder and parenteral crude liver extract have been used, because these substances were believed to contain more than the then known accessory food substances (1, 2). Some workers have advocated the use of choline (14) and intravenous liver extract (15, 16).

What may one expect from this therapy? At first there is a brightening of the patient's appearance, with sensorial clearing and increase in appetite. Diuresis may begin early in the treatment or it may not begin for several months. About 50 per cent of the patients will have a diuresis begin during the first two months of treatment (3). The process may be brisk and complete, or it may be slow with gradual replacement of fluid by tissue and without much net change in weight. Icterus clears and there is an obvious laying down of tissue. The low serum albumin level rises in favorable cases; indeed this level may be used as a valuable guide to the progress of the disease (17). Results of other tests, such as bromsulfalein retention, flocculation and thymol turbidity may show little change, despite marked clinical improvement. The time required for rehabilitation of some of these patients is usually many months. During this period, intercurrent infection or other complicating illnesses may occur, requiring definitive therapy. Occasionally a strangulated hernia, umbilical or inguinal, may need surgical treatment. Operation or any trauma is poorly tolerated; therefore, it is well to

avoid all elective surgery. However, the outlook today is greatly improved over that before the use of dietary therapy (2). The prognosis has been further brightened by the availability of antibiotics, sulfa drugs and improved anaesthesiologic and surgical techniques.

Following sustained improvement, patients may be expected to do well indefinitely, provided good nutrition with abstinence from alcohol is maintained, and provided bleeding from ruptured esophageal varices does not occur. Some patients will improve but never regain a robust state of health. These patients will usually show a sustained reduction of the serum albumin level, and the prognosis should be guarded (17). Other patients will fail to improve and succumb to the disease process.

It is well to comment upon the place of *alcohol* in this disease. There seems to be little basis for the thesis that alcohol, per se, is the cause of Laennec's cirrhosis. The disease occurs most commonly in this part of the world in alcoholics. However, it occurs in other parts of the world in persons who abstain from alcohol. It is also seen in the course of chronic wasting diseases, such as ulcerative colitis. The common denominator seems to be poor nutritional state, with particular reference to insufficient protein intake. Alcoholism may act as a conditioning factor for malnutrition, since the consumption of large amounts of alcohol is usually associated with poor food intake. The alcohol supplies calories without the food substances and vitamins needed to support the metabolic requirements. The evidence available from experimental animals suggests possible biochemical mechanisms for the development of hepatic cirrhosis in man. However, much study is needed to resolve these problems in man. During the past five years investigations have been in progress in this laboratory on the clinical, functional and histologic development of this disease in a group of chronic alcoholic subjects, in whom all evidences for liver disease were absent when first they were studied. It has been surprising to see how much alcoholism and poor food intake may be tolerated by some individuals without the development of liver disease. These studies suggest that there are other factors, as yet unknown, which are involved in the genesis of Laennec's cirrhosis of the liver.

The question is often raised whether the patient with Laennec's cirrhosis may be permitted to consume alcohol. It has been shown that it is possible for such patients to take alcohol, provided their nutritional state is well maintained. The studies were made under controlled hospital supervision (2). Because of the difficulty many of these patients have in limiting their consumption of alcohol, they have been urged to abstain completely when discharged from the hospital. Unfortunately this advice is frequently ignored and the most common cause of relapse is the resumption of poor diet and heavy drinking. Although when the clinical condition becomes worse, tolerance to alcohol is much reduced and drinking may even become loathsome, once the patients have begun to feel well it may be impossible to keep some of them from resuming their old eating and drinking customs. The problem of alcoholism is a psychiatric one and beyond the scope of this discussion.

Associated with the development of Laennec's cirrhosis is a profound col-

lateralization of the portal venous bed, with the development of varices in the esophagus, stomach, rectum and abdominal wall. The varices of the stomach and esophagus are constant threats, for bleeding from these veins is a continuing possibility and unrelated to the functional state of the liver. Why bleeding occurs when it does, or why it occurs frequently in certain patients and never in others is unknown.

Massive hemorrhage, such as that following rupture of esophageal or gastric varices, is a major crisis. There are two aspects to its gravity. The first is the immediate one of acute blood loss and possible death from shock. The second is the damaging effect of hemorrhage upon an already diseased liver. It is not uncommon for hepatic insufficiency with coma to follow such a hemorrhage. The treatment of the acute hemorrhage is the same as for any profound blood loss. The use of the esophageal balloon has been disappointing in the author's experience, with but 1 survivor among 14 patients in whom the balloon was used. In 2 patients, esophageal bleeding was controlled, but rupture of gastric varices occurred with fatal outcome. The surgical reduction of portal venous pressure has introduced a new and challenging method for the management of this grave complication of Laennec's cirrhosis. The shunt procedures have been successful in many instances and are worthwhile in patients who have suffered serious bleeding. They should be reserved for the treatment of varices which have bled, and have no place in the treatment of ascites (18, 19).

The end-stage of liver disease is *hepatic coma*. This state is characterized by one or all of the following: stupor, restlessness, tremor, bizarre neurologic findings sometimes simulating hemiplegia, deep jaundice and the "fetor hepaticus" breath. Although this state is probably a cerebral consequence of profound hepatic insufficiency, the metabolic abnormalities which characterize it are unknown (20). Thus the results of conventional liver function tests in the comatose patient may be unchanged compared with those of the same patient before the advent of coma. Coma may occur in the course of progressive hepatic insufficiency or it may be precipitated by massive hemorrhage, infection, oversedation, trauma, surgery, superimposed viral hepatitis and a heavy alcoholic debauch. When the coma has followed hemorrhage or infection, it may be treated with transfusions and antibiotics. The administration of intravenous glucose and vitamins is associated with 25 per cent survival from coma (2). More recently, intravenous salt-poor human albumin has been added to the regimen, with almost 60 per cent survival (9). Aureomycin has been recommended in this state (21). The treatment of coma still leaves much to be desired. It is likely that when the underlying metabolic faults are better understood, better therapeutic measures will be developed.

SUMMARY

1. Laennec's cirrhosis of the liver, as seen in this part of the world, is a disease most commonly associated with malnutrition and conditioned by alcoholism. A nutritious diet, with vitamin supplements, is effective in reversing the downhill course of the disease and restoring the patient to good health. The use of

mercurials, ammonium chloride, salt restriction, exchange resins and intravenous salt-poor albumin is of benefit in the management of fluid retention.

2. The problems of therapy for bleeding esophageal varices and hepatic coma have been discussed.

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COMMON BLOOD PROBLEMS IN OLDER PEOPLE*

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Many years ago it was generally thought that the blood forming tissues undergo senile changes as do many other organs, because of such factors as "wear and tear", "arteriosclerosis" and probably because there was no reason to believe that the hematopoietic system should be exempt from "the way of all flesh."

This concept was generally abandoned when convincing data failed to support such an assumption. Moreover, in many studies it was difficult to find an adequate number of aged individuals who were free of disease or malnutrition.

For example Newman and Gitlow (1) studied 50 aged males and 50 aged females presumably showing no clinical evidence of disease and concluded that normal levels of physiologic function are different when dealing with elderly individuals. They investigated hemoglobin values, red blood cell counts, fragility tests, reticulocyte counts and determined the various indices. A careful perusal of their data indicates that the values obtained were not appreciably different from those in many studies in younger groups. Moreover their work could not be controlled by studying younger normal individuals living under the same institutional conditions.

Olbrich (2) reported that the mean red blood cell diameter is distinctly larger in the aged and the scatter, measured by standard deviation and coefficient of variation, is bigger; red blood cell fragility is increased; the sedimentation rate is increased, p robably due to changes in the plasma proteins; and the polymorphonuclear cells show an increase in lobulation of the nuclei. He also concluded that the bone marrow produces cells at a diminished rate but the rate of the destruction of these cells is also diminished.

Probably the most critical study of the hematopoietic functions in normal old subjects is that of Shapleigh, Mayes and Moore (3), who investigated 50 males and 50 females aged from 60 to 95, who were free of disease other than degenerative changes. These authors believed that the bone marrow of their aged patients showed a probable tendency toward a decrease in the ratio of red marrow to fatty marrow, but normal counts were maintained. No significant changes were found in blood volume, reticulocyte or white blood cell counts, differential counts, or the factors which control hemostasis. They thought that the red blood cell, hemoglobin and hematocrit values showed a slight decrease from levels found in healthy young adults, probably more pronounced in men than in women, and that the mean corpuscular hemoglobin figures might be slightly

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lower. The sedimentation rate in about half their subjects was somewhat increased, but there were certainly no striking changes compared with the rate in younger persons.

Therefore, we must conclude that age itself produces no conspicuous alteration in the hematopoietic system.

In all patients, abnormalities of the blood and the blood forming organs are secondary to etiologic factors affecting the entire body. There is probably no true primary hematologic disorder.

The problem is, therefore, the following: of the usual hematologic disorders seen in old age, which ones are present because elderly persons are subject to certain disorders or environments because of their age, and which ones are present because such persons are aged?

Probably the most common hematologic disorder seen in old people is anemia. This condition may be due to any of the causes producing anemia in any age group. But certain influences tend to cause an increased incidence as people become older. Hypochlorhydria and achlorhydria are more prevalent and these conditions may have some influence on iron and maturative factor absorption. Appetite is decreased with less activity, and this tends to increase dietary deficiencies. If certain articles of food are eliminated, such as citrus fruits, subclinical scurvy may ensue. Neoplasms, although present in all age groups, are probably more common in the old; thus blood loss from the gastro-intestinal, urinary or genital tract is not uncommon. Moreover, neoplasms produce anemia in part by hemolytic action. Anemia is also a striking feature of uremia. In our clinic, pernicious anemia is found more commonly in patients younger than 60.

As far as other hematologic disorders are concerned, there does not seem to be any distinct prevalence in old age. Leukemia of any type is seen at all ages. Polycythemia is usually diagnosed in individuals younger than 65. Hemorrhagic states are certainly not characteristic of old people, except perhaps the senile purpura due to vascular fragility secondary to atrophic changes in the skin and subcutaneous tissue; this purpura is not common and is usually slight. Hair dyes may produce aplastic anemia or rather, hypoplastic bone marrow. The use of hair dye is more common as age begins to leave its mark; but very old people usually have lost most of their vanity and no longer need appear young in order to retain their positions.

Two important facts, therefore, must be borne in mind by the physician when he considers the hematopoietic system of the aged. First, the blood and blood forming organs are remarkably free from degenerative conditions in the older members of the community. This fact is not due to any superior skill of the hematologist as compared to the cardio-vascular specialist, but is a characteristic of the tissues with which we deal. Secondly, many disorders of the blood are seen in elderly patients (*e.g.*, anemia, leukemia, Hodgkin's disease) and therefore the physician must constantly keep in mind the fact that older people may present the same blood diseases seen in younger patients.

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THE AGING SYNDROME*

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Aging in living organisms, perhaps conditioned by hereditary factors influencing longevity, is represented by a composite of multiple and varied morbidities arising as the consequence of diminished functional, structural, local and systemic resistance to relatively harsh, internal and external environmental stimuli. Resultant pathologic conditions constitute an Aging Syndrome (A–S) which, unopposed and unaltered, leads to deterioration and demise of the individual. The present study classifies aging as a disease complex, emphasizing the etiologic significance of both internal and external environmental stress.

Incriminated as causative factors in aging, environmental stressors possessing chief culpability are: socio-economic status; occupational exposure or injuries; and traumata—of all kinds and degrees—affecting psyche and/or soma, of nutritional, infectious, toxic, biochemical, mechanical and physiologic or physio-organic origin or nature. Disturbances, alterations and disorders in regulation, equilibrium, and/or control of such factors as enzyme and colloidal systems, pH and electrolyte balance, temperature, hydration, general and mineral metabolism, can contribute markedly to the inauguration, intensification and perpetuation of the A-S. Overtaxation of defense reserves and lowered target resistance of stressed, isolated, related and combined functional and/or organic units are intimately interwoven with aging. Consideration of stressor-adaptive mechanisms should include the thought that the nature and degree of adaptation may vary with:

1) The fundamental quality, quantity and intensity, as well as the source and mode of transmission (vector) of the stressor agent.
2) The fundamental quality, quantity and intensity of resistance by the stressed target.

Thus, decreased resistance to stress and/or environmental stress of relatively overwhelming proportions may be involved, in varying degrees, according to circumstances, in causation of the A-S.

In most instances, the basic pathologic factors of the A-S are multiphasic, subclinical, of "*silent onset*" in the earlier stages, but cumulative in time, declaring themselves as outward superficial symptoms of senescence only after myriad wounds and scars have been inflicted on targets with failing resistance to invading stressors. Dominant processes are: intracellular and extracellular dehydration or desiccation, fluid reduction and/or depletion, general cellular atrophy—particularly manifest in the nervous, elastic, epithelial, vascular,

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muscular, skeletal and glandular elements—and fibrosis, or interstitial connective tissue hypertrophy and/or hyperplasia leading to increased structural density. Inflammation, sclerosis—especially atherosclerosis—ankylosis and necrosis, of multitudinous varieties, combinations and degrees, can be present in the A-S. A tendency to neoplasia and increased incidence of malignant new growths is manifest in the relatively aged. Weakening or loss of a function or structure helps to establish, accelerate and intensify additional involutionary processes in the same or other systems or organs. Insidious, subclinical, repeated and cumulative stressor insults may cause subsequent development and outward declaration and intensification of the A-S. As explained later in this presentation, the aforementioned pathologic processes probably represent maladaptation, that is, partial or complete failure of target resistance and/or relative or absolute overwhelming of basic functional and/or structural organizations by repeated stressor assaults.

Available knowledge concerning symptoms—simple, complex and highly variable—of morbidity in aging has been capably described in detail by experts elsewhere (1–5). Needless reiteration will not be attempted here; rather, suffice it to mention briefly several classic symptoms of the A-S, such as: decrease and loss of skin elasticity with thinning and wrinkling, abnormal skeletal and postural alterations, relative decline and/or loss of special sensory organ functions, decline in epithelial secretory activity and characteristic accompanying symptoms manifest principally in the respiratory, gastro-intestinal and genito-urinary tracts, progressive neuromuscular fatigue and asthenia, vasomotor and locomotor instability, and symptoms related to gonadal failure and general decline of the endocrine glands, as well as general and specific metabolic failure of different degrees. An over-simplification is the conclusion that, in all probability, no organismal component can withstand the ravages of internal and external stress in time; concomitant symptoms must, of necessity, be shaped by the relative strength of stressor versus stressed.

In other studies, abundant factual evidence has been provided by this author, in proof that relatively radical, vigorous, usually expensive, extensive therapeutic intervention may result in noteworthy rehabilitation of markedly debilitated aging and aged subjects (6–9). Individuals—in some cases apparently moribund—afflicted with conditions or disease complexes ordinarily deemed hopeless from the viewpoints of salvage or recovery, have been restored to adjusted, physical and mental well-being in their customary environments, creating unexpected measures of renewed happiness for patients and their beloved ones alike. Initial emergency measures—antibiotics, surgery, blood transfusions, digitalization, insulin in diabetes complicated or uncomplicated by coma—were subsequently supplemented or replaced by maintenance doses of hormones and vitamins, special diets, and therapy directed at improvement of the principal functional and structural systems (such as the cardiovascular, hepatic, renal, skeletal, nervous, or respiratory). In the follow-up of these patients, emphasis is placed on prophylactic rather than therapeutic measures of control.

For the purposes of this study, treatment of the A-S may be classified broadly as:

1) *Passive:* little or no active resistance to stress; the stressor effect is accepted without any attempts at adaptive response; *puerile* approach (− −); for example, fulminating, highly virulent, untreated infectious pneumonitis which becomes terminal in an host already severely debilitated by prior disease.
2) *Palliative:* attempted resistance is approximately equal to stress; there is moderation or attenuation of stressor effects; *static* approach (−); includes relatively insufficient, nonspecific measures, such as the use of analgesics and antipyretics in instances like the pneumonitis just cited.
3) *Therapeutic:* attempted resistance is greater than the immediate stress; there is relative destruction and/or elimination of stressor, but no worthy attempts at reconstruction or prevention; *aggressive* approach, partial (+ −); for example, the administration of vitamins, antibiotics and special diets during the stress and convalescence phases of an acute infectious ailment.
4) *Prophylactic:* object is to prevent stress and augment resistance to withstand probable future stressor assaults; *preventive* approach, partial (+); involves nonspecific observation of healthy dietary, occupational and living habits, good mental and social hygiene, economic and other environmental considerations, as well as the relative elimination—insofar as possible—of all potential stressor agents, their sources and means of attack.
5) *Rehabilitative-prophylactic:* there is attempted restoration and maintenance of peak specific and nonspecific resistance, with relative reduction, inhibition or circumscription of stressor impacts to limits of constructive stimulation; *dynamic-reconstructive-preventive approach* (+ +); to wit, following chronic or acute debilitation characterized by the signs and symptoms of relative aging, complete rehabilitation of the subject is sought, employing a composite of measures as outlined in sections 2), 3) and 4), in addition to the use of all practical ways and means (such as high potency vitamins and hormones) capable of stimulating and creating maximum, relatively permanent, positive, individual resistance to stress.

Combinations of the foregoing treatments are possible (*e.g.*, therapeutic-prophylactic, or therapeutic-prophylactic-rehabilitative), depending on the particular set of circumstances in each case.

At present, the theory of "normal, natural, healthy senescence" and its supposedly non-diseased pattern of progressive atrophy and decreased vitality is an imaginative figment. Little reason exists to discredit those who claim that the aging process, senescence or involution, is essentially pathologic. Many gerontologists admit that proof of "physiologic" aging is not available now, but most of these same authorities attempt, at one time or another, to distinguish between "normal senescence" and the "chronic degenerative diseases." Stieglitz (10) wrote: "even pathologists are unable to distinguish which structural changes in senility are due purely to aging and which result from accumulative injury. . ." He separated the chronic "degenerative" diseases into four major categories (circulatory impairments, metabolic dysfunctions, arthritides and neoplasms), attesting to the increasing frequency of these maladies in advancing years,

ascribing causation of almost 60 per cent of all present-day deaths in the U. S. to sickness in this group. Boas (11) stated that postmortem examinations in older individuals always reveal a pathologic cause of death, even when no symptoms were observable during life. Other studies have yielded the following facts: The age bracket from 15 to 64 years contains more than three quarters of the chronically sick, at least 50 per cent of the afflicted being less than 45 years of age (12). Between 55 and 74 years of age, cardiovascular disease accounts for 52.1 per cent of deaths from all causes; and after 75 years of age, 60 per cent. In general, cardiovascular diseases caused over half of all deaths, and arteriosclerosis and hypertension caused over 90 per cent of all deaths from cardiovascular diseases in the U. S. in 1950 and 1951 (13). Deaths after the age of 65 are caused most commonly by coronary, cerebral or peripheral arteriosclerosis, hypertension, carcinoma of the gastro-intestinal tract, prostatic hypertrophy, tuberculosis and street accidents (11). Thus, while real diseases cause characteristic symptoms and eventual destruction of aging and aged hosts, a procession of "believers" kneels respectfully in front of the symbolic altar of a mysterious "normal aging process."

Though a suspected, as yet poorly defined hereditary longevity potential is believed to limit man's existence (14), the marked impact of internal and external environment has long been recognized as potent in the causation of disease associated with senescence and death (Fig. 1). Breslow (15) felt that mounting evidence supported the view that physical and social environmental conditions are the decisive factors in the etiology of chronic diseases. Selye (16) suggested that collagen diseases "may represent a process of 'accelerated aging' similar to the normal aging which occurs under the influence of the stresses and strains of daily life." Vischer (17) took cognizance of environmental impress, remarking that ". . . every individual reveals, in advanced age, the traces of his own life history. . ." Stieglitz (10) emphasized the importance of the marked impression left by cumulative "scarring" due to the "inevitable and innumerable minor and major insults to which everyone is subject. . ." Loeb (18) interpreted the processes leading to organismal decline—the tendency to disease, aging and death—as manifestations of the lack of perfect adaptation between constituent parts within organisms, and between organisms and their environment, nonadapted organisms being eliminated. He reasoned that primitive forms of life—cells and their compositions into simple structural and functional organizations—are endowed with the potential of endless longevity, limited only by environmental boundaries. Further, in the course of evolution to higher organismal levels, the figurative price paid for development, refinement and individuality was the sacrifice of this theoretical birthright to eternal life. This concept was postulated in consideration of the context of an hypothetical environment which never existed, actually, for the bulk of life since its inception on this planet; otherwise, the entire course of historical evolution might have been altered.

In his monumental description of the General-Adaptation-Syndrome (G-A-S), Selye (19) demonstrated that during prolonged systemic stress of the animal body, specific biochemical, morphologic and physiologic targets of systemic stres-

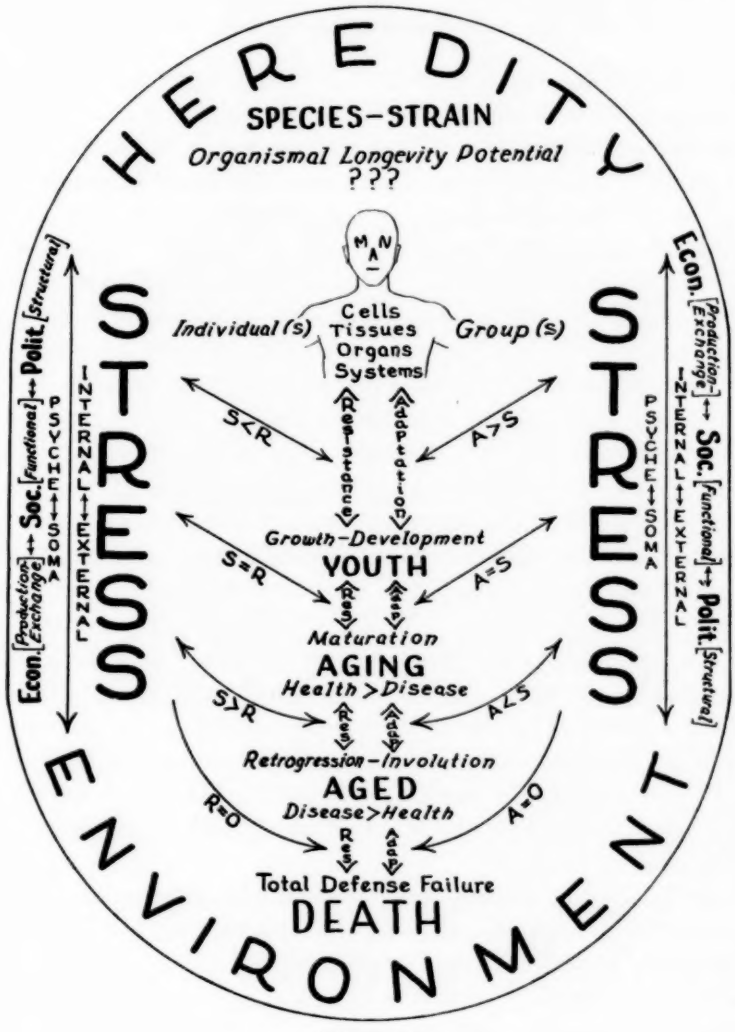

FIGURE 1

sors responded with changes following a general, characteristic, triphasic course of alarm, resistance and exhaustion. The same stressor agent is capable of evoking opposite effects—stimulus or stress—depending upon the qualitative and quantitative previous exposure of the target to stressor stimulation. The G-A-S, in effect, aids adaptation which, in turn, can cause disease resulting from maladaptation ("hypo-, hyper- or dysadaptation"). Among the diseases of adaptation, Selye included: "... some of the most common fatal diseases of Man, such as the hypertensive, the 'rheumatic' and the 'degenerative' or 'wear-and-tear' diseases of old age; the psychosomatic syndromes probably also belong to this group." Since his definition of "stressors" includes all pathogens, and all diseases are effected out of the struggle between pathogen and organism, Selye wrote: "it is obvious that—apart from instant death (*e.g.*, that caused by a lesion to a vital center)—some manifestations of the G-A-S will accompany all pathologic processes (20)."

DISCUSSION

If the most distinctive characteristic of life is probably adaptability, as Selye (21) and Jensen (22) believed, it should follow that the emergence of higher evolutionary forms of life, particularly man, resulted from environmental conditioning and adaptive reactions. Organismal refinement and augmented specialization of function and structure should, hypothetically, result in a prolonged and not shortened life-span. This reasoning finds confirmation in an ever-growing world population, indicating that the human species is still in a relatively healthy phase of evolutionary growth and development, probably reflecting mankind's increasing resistance and control of many infectious diseases which were formerly considered fatal. Contributing considerably to the betterment of the overall picture is an enlightened insight into the important roles which environmental and socio-economic factors play in disease causation. Increasing knowledge of this nature provides powerful weapons for battling against basic stressors in aging and augmenting host resistance to such stressors. Man's extensive mental capacity should enable him, ever-increasingly, to harness and mold the forces of nature and environment, adjusting and adapting these at will, in order to ease stress and improve the human lot. In time, travel in this progressive direction should lead to the nearly ideal environment necessary for the attainment of maximal potential, healthy longevity. Experience lends credence to this train of thought, for adaptation to environmental stress is more readily accomplished via knowledge and understanding leading to positive constructive action than through the faculty of brute resistance alone; furthermore, man's conquests and discoveries in the scientific and socio-economic realms are vast in life-saving and life-prolonging import.

Recognition that aging is the composite superficial expression of multiple underlying chronic and/or acute pathologic processes should lead to the challenge of certain currently popular notions in gerontology, *viz.*, that aging phenomena are "normal and inevitable." With the negation of such unscientific but traditional beliefs, static, passive and relatively ineffectual approaches to medical problems of aging and the aged will be swept away by a flood of highly positive, therapeutic, reconstructive, rehabilitative, and preventive approaches in geriatrics.

The obvious ultimate aim in gerontology should be to realize this ideal of perfection: maintenance of the entire human economy at its full peak of youthful, functional and structural vigor. Further definition, development, elaboration and emphasis of the tenet that aging is, essentially, a syndrome constituted by combinations of widely varying disease processes—the result of environmental impact on failing resistance and an undetermined longevity potential—will greatly stimulate progress in the direction of the ideal goal.

SUMMARY

Data are furnished to develop the thesis that aging in man is, essentially, a disease syndrome arising out of the struggle between environmental stress

versus biologic resistance and relative adaptation to the effects of stressor agents.

Acknowledgment

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POSTOPERATIVE MORTALITY IN THE AGED*

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The purpose of this preliminary report is to review the causes of postoperative mortality in elderly patients. The case records have been studied from the standpoint of types of operative procedures performed, diagnoses and complications.

The material presented in this report is taken from the case records of 60 patients who expired postoperatively. A total of 934 patients over the age of 60 were operated upon in the year 1951 at the Veterans Administration Hospital, Hines, Illinois. These 934 cases represent approximately 10 per cent of the total number of patients operated upon during the year.

An attempt has been made to classify the conditions existing at the time of death. Case records were reviewed to determine the following factors:

1. Time relation of death to operation.
2. Whether the operation was an elective one, or whether it was an emergency procedure.
3. Whether the immediate cause of death was natural progression of disease (unrelated to the operative technic), or the operation itself or complications thereof.
4. The relationship of underlying disease to postoperative death.

Later papers will deal with operative complications in the group as a whole and with the incidence of morbidity in these aged patients.

It is emphasized that this is not a statistical report, but a summary and review of the available material. The patients studied were all men, since the veteran population is predominantly male. This series of cases, then, does not represent an adequate cross-section of the geriatric population, but probably is more typical of the veteran population.

The figures presented agree remarkably well in overall percentages with those presented by Strohl and Diffenbaugh (*J. Am. Ger. Soc.* **1:** 771, 1953), and accordingly it is felt that they may be of some value.

The uncorrected mortality in geriatric surgical patients was 60 deaths in 934 cases or 6.42 per cent (Table 1). Although no attempt is made to imply a distinction between surgical and nonsurgical deaths, such a division has been made for purposes of analysis, to show that some of these deaths may have been preventable. When the circumstances of the deaths were investigated it was seen that 28 of the 60 were from causes completely unrelated to the surgery performed. This left 32 cases in which death was in some way related to surgery, making a corrected mortality rate of 3.4 per cent—considerably lower than that

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TABLE 1

Mortality in Geriatric Surgical Patients

(934 cases—approximately 10 per cent of all surgical cases)

	No.	During postop. days 1–14	During postop. days 15 plus	Per cent of geriatric cases
Postoperative deaths	60	32	28	6.42
Deaths unrelated to surgery	28	6	22	3.00
Deaths related to surgery	*32*	*26*	*6*	*3.42*
Operative deaths	21	16	5	2.24

TABLE 2

Mortality Related to Status of Operation

(934 geriatric cases)

	No.	Per cent of geriatric cases	No. related to surgery	Per cent of geriatric cases
Deaths following elective operations	4	0.42	2	0.21
Deaths following nonelective operations	56	5.99	30	3.21

popularly attributed to surgery in the aging patient. Of the 32 deaths related to surgery, 21 were considered operative deaths (*i.e.*, operation contributed to some degree to the immediate rather than to the proximal cause of death), making an operative mortality of 2.24 per cent.

There were 4 patients who died following elective surgery (Table 2). In 2 of these, death was related to surgery—a rate of 0.21 per cent of all patients in this age group. Fifty-six patients expired following urgent nonelective surgery, and 30 of these deaths were related in some way to the operative procedure. In analyzing operations which were followed by death of the patient (Table 3) it was

TABLE 3

Mortality Related to Types of Operative Procedure

(934 geriatric cases)

	Total No. of deaths	Deaths related to surgery	Deaths unrelated to surgery
Urologic procedures	17	12	5
Major laparotomy	15	10	5
Thoracotomy	10	5	5
Neurologic surgery	7	2	5
Amputations	6	2	4
Biopsies	2		2
Orthopedic surgery	1	1	
Sympathectomy	1		1
Hemorrhoidectomy	1		1
Total	60	32	28

TABLE 4

Primary Causes of 28 Deaths not Related to Surgery in 934 Geriatric Surgical Patients

Carcinomatosis	10	Urinary tract infection	2
Hemorrhage (from carcinoma)	4	Brain tumor	2
Cerebral vascular accident	2	Pulmonary tuberculosis	1
Bronchopneumonia	2	Superior vena cava thrombosis	1
Gradual deterioration	2	Aortic thrombosis	1
		Coronary infarction	1

TABLE 5

Primary Causes of 32 Deaths Related to Surgery in 934 Geriatric Surgical Patients

Peritonitis	7	Brain tumor	1
Vascular accident	6	Ileus	1
Hemorrhage	4	Shock	1
Septicemia	3	Brain stem hemorrhage	1
Hepatorenal syndrome	2	Uremia; coronary infarction	1
Hepatitis (following transfusions)	2	Pneumonia	1
Acute respiratory collapse	2		

strikingly apparent that urologic procedures, major laparotomies and thoracotomies accounted for most of the postoperative deaths. This is not surprising, in view of the fact that in this hospital operations of these types are the ones most frequently performed upon patients of the older age groups.

In studying the cause of death in the 28 patients whose demise was unrelated to the operative procedure (Table 4), it is seen that neoplastic disease accounted for 16 of the 28 deaths, and vascular diseases for 5 of the remaining 12.

The 32 patients whose deaths were related to the operation showed a somewhat different distribution of the cause of death. In Table 5 it is seen that peritonitis is the most frequent cause of death, with vascular accidents, hemorrhage and septicemia following close behind. This would indicate that the geriatric patient is more fragile than the younger adult. His cardiovascular system is more vulnerable to insult and his protective mechanisms against infection are lowered. It is significant that among the 7 patients who died of peritonitis, 4 of the deaths were associated with leakage after some type of gastrointestinal tract anastomosis. In the remaining 3 cases, peritonitis was due to a perforated abdominal viscus prior to operation.

Six patients died of vascular accidents. This demonstrates the fact that in elderly individuals, because of the frequency of arteriosclerosis, the cerebral circulation is more likely to be disturbed by variations from homeostasis.

Four patients died from postoperative hemorrhage. This is more than ordinarily significant, in a hospital where blood is easily obtainable and used as indicated. In each of these cases efforts at replacement were made; nevertheless, death ensued.

Septicemia accounted for 3 deaths. These were all in debilitated patients who had undergone urologic procedures and were overwhelmed by their genitourinary tract infections in spite of energetic antibiotic and other therapy.

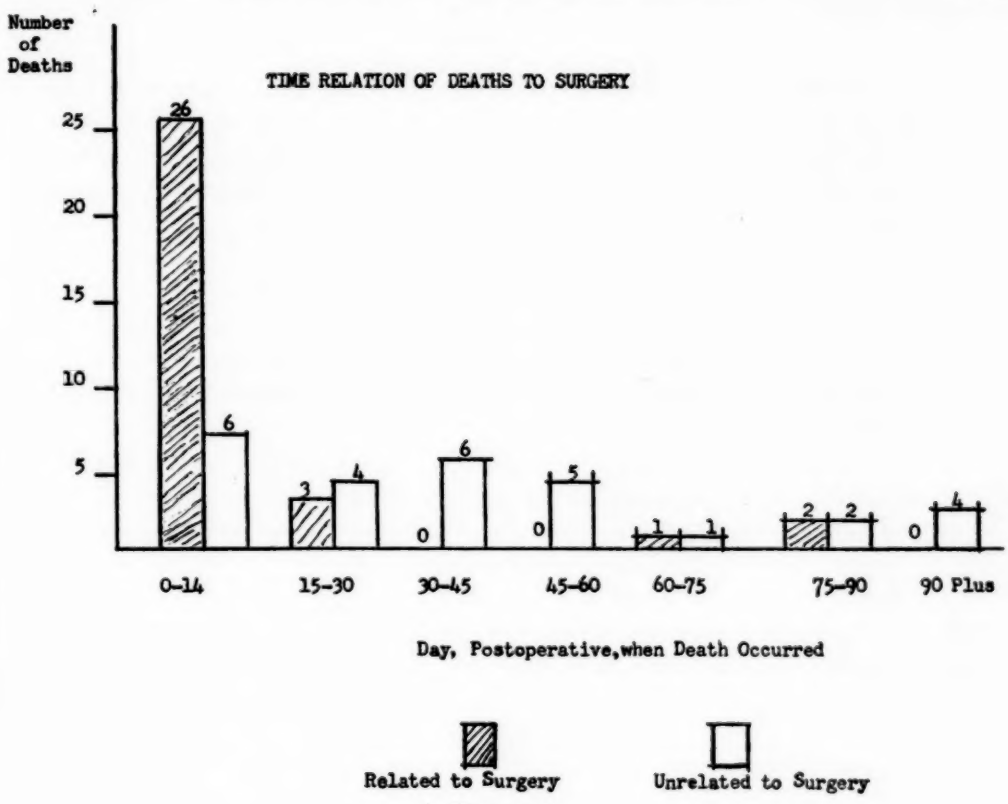

FIGURE 1

The fact that 2 patients died of hepatitis caused by delayed reactions to transfusions of blood is very interesting, for it tends to emphasize again that the giving of blood to any patient is not an innocuous procedure and may prove fatal. Two deaths from this cause in a series of 934 patients is an incidence worthy of note.

Figure 1 shows the time relationship of operation to death in the two groups of patients. It is noted that a significant difference exists between the distribution in the two groups. The majority (26) of the deaths related to surgery occurred within fourteen days after operation. The deaths unrelated to surgery were fairly evenly distributed throughout the postoperative period. The figures for the individual days during the first two weeks are not presented, as there was no significant variation.

COMMENT

It is important not to lose sight of the fact that the overall surgical death rate in this series of 934 cases was only 3.4 per cent, and that only 32 deaths were related to surgery in a series of almost 1,000 men over the age of 60. These men underwent all types of operation, varying from biopsy to such major procedures as esophago-jejunostomy with splenectomy, total gastrectomy and partial esophagectomy. (In another study of 260 cases over the age of 65, our statistics showed 15 deaths related to surgery, making a mortality rate of 5.6 per cent).

SUMMARY

From an analysis of the causes of death following surgical procedures in 934 men of the geriatric age group, the following conclusions have been drawn:

1. The difference in both type and gravity of the operations, compared with those usually performed on younger men, precludes comparison with mortality statistics in that age group. In the geriatric group there is a preponderance of operations for malignancy and for obstructive urinary phenomena, whereas in the younger group, elective operations predominate.

2. The geriatric patient need not be considered an increased surgical risk. A mortality rate of 3.4 per cent for death related to the operative procedure, in a series of almost 1,000 aging men, is lower than ordinarily anticipated for an over-60 age group.

3. The causes of postoperative death in older patients vary considerably. Overwhelming infection, vascular accidents and hemorrhage account for most deaths associated with operation, whereas malignancy and vascular disease are the causative factors in the nonoperative deaths.

4. Deaths related to surgery occur most frequently in the first two weeks following operation, whereas deaths which are only incidentally associated with surgery show no such time relationship.

AMERICAN GERIATRICS SOCIETY

THE 1954 ANNUAL MEETING

The 11th Annual Meeting of the American Geriatrics Society will be held at the Hotel Fairmont in San Francisco just preceding the meeting of the American Medical Association. The scientific sessions of the meeting will begin Thursday afternoon, June 17 and continue through Saturday morning, June 19.

Hotel reservations should be made through the San Francisco Convention and Visitors Bureau, 200 Civic Auditorium, San Francisco 2, California. Members should reserve accommodations immediately, stating times of arrival and departure, because the hotels expect to be filled to capacity.

The Annual Business Meeting will be held in the Fairmont Hotel Thursday morning, June 17, at 9 o'clock. The room for this meeting will be announced later. All Scientific Sessions will be held in the Nob Hill Room of the Fairmont, and the annual dinner is scheduled for the Terrace Room on Friday evening, June 18.

The meeting will be open to all members of the American Geriatrics Society and to physicians and other scientists who are interested in the field of geriatrics. The program will cover many aspects of geriatric medicine, and there will be several panel discussions on such subjects as recent developments in cardiology, methods of determining operability in older patients, and the relation of industry to geriatrics. Outstanding clinicians and investigators will participate.

Dr. Laurance W. Kinsell, Highland Alameda County Hospital, 2701 Fourteenth Avenue, Oakland 6, California, is in charge of local arrangements for the meeting.

W. O. Thompson, M.D.
President

ADDITION:

PROVISIONAL PROGRAM

July 19, A.M. Meeting of the Governing Body.
July 19, P.M. Official opening of Conference, followed by meetings of the Sectional Committees.
July 20, 21 and 22. Scientific Meetings of the Conference.
July 23. Closing Meetings of the Conference.

The meetings and discussions will be divided between three main sections of the Conference:

Section 1. Biology and Pathology.
Section 2. Geriatric Medicine and Psychiatry.
Section 3. Sociology and Psychology.

Discussions and symposia involving combined meetings of two or more sections, and meetings of the Research Group, are to be arranged.

Visits

Visits will be arranged during the meeting in London, to centers in and around London. After the Congress, tours will be arranged to other centers in the United Kingdom.

Opportunities will be given to members to see geriatric units in hospitals, residential homes, housing accommodations, clubs and special industrial facilities.

Proposed Provincial Tours

Following the main Congress, tours will be arranged to enable members to see something of the work for the elderly throughout the country. Local members have expressed the wish to meet members attending the Congress and to entertain them during the provincial visits.

The following tours are being arranged: 1). London, Oxford, then to the West Country, returning via Southampton and Salisbury to London. 2). London, Nottingham, Sheffield, Leeds, Harrogate, Durham, Sunderland, York, Lincoln and Cambridge, to London.

Social Occasions

July 19. President's Reception in the evening.
July 21. Evening Reception.
July 23. Conference Dinner.

Throughout the Congress, visits to centers of scenic and historic interest in and around London will be arranged. Opportunities will also be provided for members to meet informally.

AMERICAN GOITER ASSOCIATION

The Annual Meeting of the American Goiter Association will be held at the Somerset Hotel, Boston, Massachusetts, April 29, 30 and May 1, 1954. The program for the three-day meeting will consist of papers and discussions dealing with thyroid physiology and disease.

Hotel reservations should be made by writing to Mr. Harry Hoghn, Executive Assistant Manager, The Somerset, 400 Commonwealth Avenue, Boston 15, Massachusetts.